VOLUME 18 *Baltimore Number* NUMBER 6

THE MEDICAL CLINICS OF NORTH AMERICA

MAY, 1935

Index Number

PHILADELPHIA AND LONDON
W B SAUNDERS COMPANY

PUBLISHED BI-MONTHLY (SIX NUMBERS A YEAR) BY W. B. SAUNDERS COMPANY WEST WASHINGTON SQUARE PHILADELPHIA.

MADE IN U. S. A.

CONTRIBUTORS TO THIS NUMBER

CHARLES R. AUSTRIAN, M. D., Associate Professor of Medicine, The Johns Hopkins University; Assistant Visiting Physician, The Johns Hopkins Hospital; Physician-in-Chief, Sinai Hospital.

LEWELLYS F. BARKER, M. D., Professor Emeritus of Medicine, The Johns Hopkins University; Visiting Physician, The Johns Hopkins Hospital.

E. W. BRIDGMAN, M. D., Associate in Medicine, The Johns Hopkins University; Assistant Visiting Physician, The Johns Hopkins Hospital; Physician-in-Charge, The Johns Hopkins Medical Dispensary; Consultant in Internal Medicine, the U. S. Public Health Service.

EDWARD P. CARTER, M. D., Adjunct Professor of Medicine, The Johns Hopkins University; Associate Physician, The Johns Hopkins Hospital.

PAUL W. CLOUGH, M. D., Associate in Medicine, The Johns Hopkins University; Assistant Visiting Physician, The Johns Hopkins Hospital.

JULIUS FRIEDENWALD, M. D., Professor of Gastro-enterology, University of Maryland.

T. B. FUTCHER, M. B., Associate Professor of Medicine, The Johns Hopkins University.

ROBERT W. JOHNSON, Jr., M. D., Associate in Orthopedic Surgery, The Johns Hopkins University; Chief of Orthopedic Dispensary Clinic and Visiting Orthopedic Surgeon, The Johns Hopkins Hospital; Assistant Medical Director, Children's Hospital School.

WILLIAM S. LOVE, Jr., M. D., Assistant Professor of Medicine, University of Maryland; Attending Physician, University Hospital; Chief of Heart Clinic, University Hospital Out Patient Department.

WALTER C. MERKEL, M. D., Pathologist and Director of Laboratories, Union Memorial Hospital; Associate Professor of Pathology, University of Maryland; Consultant Pathologist, Mercy Hospital.

SYDNEY R. MILLER, M. D., Associate in Medicine, The Johns Hopkins University; Associate Professor of Medicine, University of Maryland.

SAMUEL MORRISON, M. D., Associate in Gastro-enterology, University of Maryland.

THEODORE H. MORRISON, M. D., Associate Professor of Gastro-enterology, University of Maryland.

ESTHER LORING RICHARDS, M. D., Associate Professor of Psychiatry, The Johns Hopkins University; Physician in Charge, Henry Phipps Psychiatric Dispensary, The Johns Hopkins Hospital.

HELEN B. TAUSSIG, M. D., Instructor in Pediatrics, The Johns Hopkins University; In Charge of Heart Clinic of the Harriet Lane Home, 1930.

RICHARD W. TE LINDE, M. D., Associate in Gynecology, The Johns Hopkins University; Assistant Visiting Gynecologist, The Johns Hopkins Hospital.

HENRY M. THOMAS, Jr., M. D., Associate in Medicine, The Johns Hopkins University; Physician in Charge, The Johns Hopkins Hospital Medical Out Patient Department; Assistant Visiting Physician, The Johns Hopkins Hospital.

CONTENTS

	PAGE
SYMPOSIUM ON TREATMENT OF HEART DISEASE	1505
Angina Pectoris and Coronary Thrombosis By DR LEWELLYS F BARKER	1507
Treatment of Acute Inflammation of the Heart By DR CHARLES R. AUSTRIAN	1515
Treatment of Syphilis of the Heart and of the Coronary Arteries By DR. WILLIAM S LOVE JR	1533
The Treatment of the Different Forms of the Irregularity of the Heart (Cardiac Arrhythmias) By DR. E W BRIDGMAN	1545
The Management of Children with Rheumatic Heart Disease (Compensated and Decompensated) By DR HELEN B TAUSSIG	1559
The Use of Digitalis in Various Conditions By DR. EDWARD P CARTER	1579
Diagnosis and Treatment of Diabetes Insipidus By DR T B FUTCHER	1597
Value, Indications Limitations and Technic of Colonic Irrigation By DRS. JULIUS FRIEDENWALD and SAMUEL MORRISON	1611
Idiopathic Ulcerative Colitis with a Report of an Unusual Case By DR. THEODORE H MORRISON	1631
Behavior Problems of the Pediatrician By DR. ESTHER L RICHARDS	1663
Arthritis in Children By DR. ROBERT W JOHNSON JR	1673
The Present Status of Vital Capacity as a Test of Pulmonary Efficiency By DR HENRY M THOMAS JR	1685
The Clinical Significance of Leukorrhea and Its Treatment By DR R W TE LINDE	1697
The Treatment of Fusospirochetal Infections (Vincent s Disease) By DR. PAUL W CLOUGH	1711
Pulmonary Actinomycosis By DRS SYDNEY R. MILLER and WALTER C MERKEL	1725
Index to Volume 18	1743

Baltimore Number

THE MEDICAL CLINICS OF NORTH AMERICA

Volume 18 May, 1935 Number 6

SYMPOSIUM ON TREATMENT OF HEART DISEASE

THE following clinics are included in this Symposium

Lewellys F Barker ANGINA PECTORIS AND CORONARY THROMBOSIS

Charles R Austrian TREATMENT OF ACUTE INFLAMMATION OF THE HEART

William S Love Jr TREATMENT OF SYPHILIS OF THE HEART AND OF THE CORONARY ARTERIES.

E. W Bridgman THE TREATMENT OF THE DIFFERENT FORMS OF THE IRREGULARITY OF THE HEART (CARDIAC ARRHYTHMIAS)

Helen B Taussig THE MANAGEMENT OF CHILDREN WITH RHEUMATIC HEART DISEASE (COMPENSATED AND DECOMPENSATED)

Edward P Carter THE USE OF DIGITALIS IN VARIOUS CONDITIONS

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR LEWELLYS F BARKER

BALTIMORE

ANGINA PECTORIS AND CORONARY THROMBOSIS

MEDICAL men who have passed middle life will recall that from the senior year in the medical school onward they were made familiar with the symptoms of angina pectoris in typical cases and had no difficulty in the recognition of such cases in their practice Coronary thrombosis, however, they heard nothing about clinically though they may occasionally have seen it in the autopsy room It is only during the past few years that the attention of clinicians has been called to reliable methods of recognizing the occurrence of coronary thrombosis during life Today, every student in his clinical years in the medical school has his attention drawn to the particular clinical features of coronary thrombosis and is shown how to differentiate it from conditions that more or less simulate it

ANGINA PECTORIS

In a typical severe attack of angina pectoris the physician has as a rule, no difficulty whatever in recognizing its nature for the symptoms are very characteristic The patient is usually seized suddenly with a severe retromanubrial pain, the attack usually following exertion or excitement In some cases the actual pain is preceded by a feeling of oppression and is accompanied by a definite sense of constriction in the chest. Radiation of the pain down the medial side of the left arm and forearm to the little finger is common less often there is radiation into the right upper extremity, into the head and neck, into the upper abdomen, or into one of the thighs The attack is accompanied by a feeling of great anxiety, the patients after

wards saying that they felt that they were about to die These feelings of anxiety may be disturbing even in attacks in which the pain is not so very severe

If the physician happens to see the patient in the attack, he will be struck by the ashy pallor of the face, the desire to remain absolutely still with avoidance of all movements, and a tendency to break out into profuse perspiration The duration of an attack may vary much In some instances the symptoms last for only a few moments, in others the duration is much longer, even as long as an hour, during which there are remissions and exacerbations of the symptoms The attacks are not accompanied, as a rule, by dyspnea, tachycardia, vomiting or signs of collapse In some patients the blood pressure rises a little during an attack

The malady is much more common in men than in women Though angina pectoris may occur in the forties, the average age of onset is in the fifties and the average duration of life after onset is, roughly, four and a half years, though some die in the first attack and some live longer than a decade after the first attack Sudden death in an attack is not uncommon Not infrequently coronary thrombosis is the cause of death when the exitus occurs during an attack or shortly afterward Only about 10 per cent die of congestive heart failure following attacks

In differential diagnosis, it is the atypical cases of angina pectoris only that give any trouble When the pain radiates into the abdomen, an attack of gallstone colic or renal colic may have to be considered In a first attack of angina pectoris one must be sure to rule out pericarditis by physical examination In a few cases, severe intercostal neuralgia has been confused with angina pectoris Hysteria is, as a rule, easily ruled out by the silence and immobility of a patient during an attack of angina pectoris The differentiation from actual coronary thrombosis will be referred to when the latter subject is dealt with

Attacks of "pseudo-angina pectoris" due to the excessive use of tobacco, coffee or tea have been described, and in some

instances remarkable recoveries from what was believed to be true angina pectoris have followed abstinence from tobacco or from coffee But one should certainly be very guarded in giving a prognosis even when he suspects that true angina pectoris does not exist especially when the symptoms strongly suggest it.

In the treatment of an attack of angina pectoris nitroglycerin often gives satisfactory relief A tablet of $\frac{1}{100}$ grain (0 6 mg) may be dissolved under the tongue the moment the pain starts Many anginal victims always carry a small vial of the tablets in their waistcoat pocket. The patient should be sure that he has a reliable preparation of nitroglycerin Usually the hypodermic tablets are the most satisfactory

Some patients prefer to carry with them ampules, or pearls, of amyl nitrite, breaking one into a handkerchief and inhaling the fumes immediately If an attack occur in a physician's office or in a hospital, a hypodermic injection of $\frac{1}{4}$ grain of morphine may be given promptly, usually with good results A light, hot water bag over the precordial area is sometimes ameliorative The patient should, of course, be kept absolutely quiet until the attack has subsided

In the intervals between attacks, the patient's life should be carefully regulated Overexertion and emotional stress should be sedulously avoided The diet should be simple and easily digestible and constipation should be prevented As a rule, tobacco should be prohibited Some patients seem to have fewer attacks if they take theocalcine or some similar preparation regularly The patient's own observations as to the conditions that precipitate attacks should be carefully enquired into

During recent years surgical intervention has been resorted to in many cases of angina pectoris Some success has followed section of the posterior root of the spinal nerves from the eighth cervical to the fourth thoracic In other cases benefit has been obtained by extirpation of the superior cervical ganglion of the sympathetic or by severing both depressor nerves Recently, paravertebral injections of 0 5 per cent

solution of novocain or of 20 to 50 cc of a mixture of amidopyrine 4, aspirin 2, eucaine 0 01, sterile distilled water 100 cc , into the superior cervical ganglion While good results have been reported in certain cases, others have not been benefited Even though the pains disappeared attacks of dyspnea and of pulmonary edema developed in some cases, with exitus The most recent method of surgical intervention in angina pectoris has been by total thyroidectomy This method of treatment is so new that a period of time must elapse before its value can be determined

Many theories as to the origin of attacks of angina pectoris have been put forward Thus, in the first place, the so-called *coronary theory* has been widely accepted, it assumes that there is sclerosis of the coronary arteries with narrowing of their lumina, accompanied often by spasm, the pain arising directly in the diseased artery Others adopt an *aortic theory*, believing that the pain is due to distention of a diseased aorta or to sudden stasis of blood in the root of the aorta and the proximal portions of the main trunks of the coronary arteries A third group adopts the *heart wall theory* that assumes that pain in an attack arises in the walls of the heart in some local area that is not receiving enough blood to meet the local demand for blood and so serves as a warning to the patient This view that the pain in angina pectoris is to be attributed to temporary anoxemia of areas of the heart wall seems to be receiving ever more adherence

CORONARY THROMBOSIS

Though pathologists had recognized and described the occurrence of coronary thrombosis in cadavers a half century ago, the clinical recognition of coronary occlusion is of much more recent date It was not until 1910 and 1911 that adequate descriptions of the clinical symptoms and physical signs appeared in the German literature In America, Herrick was the first, in 1912, to lay stress upon the fact that thrombosis of a coronary artery could be quite clearly recognized during life Despite these early contributions to the clinical side of the

subject, it was not until 1918 that clinical interest became actively aroused in coronary thrombosis Dr Cary Eggleston has called attention to the fact that George Dock recognized the condition during life in one patient and confirmed it at autopsy as early as 1896 In recent years American physicians have made important contributions to the subject.

Coronary thrombosis rarely occurs before the age of forty Between forty and fifty it is not rare but it is more common after fifty Levine, in a total of 145 cases, found only three instances between the ages of thirty and thirty nine As with angina pectoris, coronary thrombosis is much more common in men than in women, apparently because of the increased incidence of arteriosclerosis and chronic arterial hypertension in men as compared with women In most incidences attacks of coronary thrombosis have been preceded by typical attacks of angina pectoris for a shorter or longer period

The clinical symptoms in typical cases of coronary thrombosis present a rather marked contrast to those of ordinary angina pectoris Thus the pain of coronary thrombosis may come on entirely independently of exertion or emotion, it may begin even when a patient is asleep, and it usually lasts much longer than the pain of ordinary angina pectoris Moreover, instead of being predominantly retromanubrial, the pain is more often situated behind the lower part of the sternum or in the upper abdomen It is, however, accompanied by anxiety and a sense of impending death very much as in angina pectoris The patient in an attack of coronary thrombosis does not, however, remain quiet but is, on the contrary, restless and may even attempt to walk about The type of pain that is associated with thrombosis is that which corresponds to the "status anginosus" of the older textbooks It is accompanied by tachycardia, enfeeblement of the heart sounds, and, after a short time, by a fall of blood pressure The patient becomes very weak, breaks out into a cold sweat and shows other symptoms of collapse Usually after a few hours slight fever with polymorphonuclear leukocytosis develops and sometimes a pericardial friction rub becomes audible The pain does not yield

to nitroglycerin or amyl nitrite, though it can be ameliorated by large doses of morphine administered hypodermically

In most cases the condition can be recognized from the symptoms alone, though in very mild instances in which there may be doubt as to the differential diagnosis between coronary thrombosis and ordinary angina pectoris, an electrocardiogram will usually give the decision If a tracing be made after twelve or twenty-four hours have elapsed, the R-T interval of the curve will usually be found markedly raised in leads I and II, with a rounded convexity upward This is the characteristic finding when the anterior descending branch of the left coronary artery has been occluded and has caused acute infarction After two or three weeks the T wave often becomes inverted, the R-T line still bulging somewhat upward For the alterations in the electrocardiogram when other branches are thrombosed and for those that persist long after an infarction has occurred the special literature may be consulted

A patient suffering from an attack of coronary thrombosis should be kept absolutely quiet in bed, preferably in a hospital and with special nursing, enough morphine should be given to control the very severe pain during the first two or three days, after which codeine may suffice Heat should be applied to the precordial region and a hot-water bag should be kept at the feet Very little nourishment should be allowed during the first twenty-four hours Then a little milk every two hours may be given and, later on, five small feedings daily of semi-solid food and milk If there be constipation, the bowels should be moved by enema

In order to permit the infarction to heal, the patient should be kept quiet in bed for at least six or eight weeks after onset This prolonged rest also helps to prevent the development of cardiac aneurysm or even rupture of the heart The prognosis given to the family should be very guarded When the patient has had attacks of ordinary angina pectoris before, it should be explained to the family how much more serious is an attack of coronary thrombosis The physician does his best,

of course, however, not to alarm the patient himself, though he must insist upon acquiescence in the measures he prescribes

SELECTED RECENT REFERENCES

Allan, W Relation of arterial hypertension to angina pectoris and coronary occlusion statistical study South. Med and Surg 96 377–379 1934

Barker P S Wilson F N., and Coller F A Abdominal disease simulating coronary occlusion Amer Jour Med. Sci 188 219–224 1934

Blumgart H. L. Levine S A., and Berlin D D Congestive heart failure and angina pectoris therapeutic effect of thyroidectomy on patients without clinical or pathologic evidence of thyroid toxicity Arch. Int. Med 51 866–877 1933 *see also* Ann Int Med., 7 1469–1477 1934

Eppinger E C., and Levine S A Angina pectoris some clinical considerations with special reference to prognosis Arch Int. Med., 53 120–139 1934

Hay J Certain aspects of coronary thrombosis Lancet London 2 787–795 1933

Hamman L Remarks on the diagnosis of coronary occlusion Ann Int Med., 8 417–431 1934

Herrick J B Clinical recognition of acute coronary thrombosis Nebraska Med Jour., 19 282–288 1934

Levy R L. Management of patient with anginal pain New England Jour Med., 211 392–397 1934

Levy R L., Bruen H G., and Kurtz, D Facts on disease of the coronary arteries, based on a survey of the clinical and pathological records of 762 cases. Amer Jour Med Sci 187 376–390 1934

Nachlass I W Pseudo-angina pectoris originating in cervical spine Jour Amer Med Assoc., 103 323–325 1934

Parade G W Die arterielle Blutversorgung des Herzens und ihre Storungen Ergebn d inn Med., 45 337–432 1933

Riesman D and Harris, S E Disease of coronary arteries with considera tion of data on the increasing mortality of heart disease Amer Jour Med. Sci 187 1–15 1934

Weinstein A A., Davis, D., Berlin D D., and Blumgart H L., Mechanism of early relief of pain in patient. with angina pectoris and congestive failure after total ablation of normal thyroid gland Amer Jour Med Sci 187 753–773 1934

Medical Clinics of North America
May 1935 Baltimore Number

CONTRIBUTION BY DR CHARLES R AUSTRIAN

BALTIMORE

TREATMENT OF ACUTE INFLAMMATION OF THE HEART

THE heart, like all other organs of the body, may be the site of inflammatory disease but it is seldom if ever a primary locus of infection Those instances of carditis, complete or incomplete, that at a glance seem to be manifestations of cardiac disease alone will be found on more careful study to represent the major or even the sole evidences of an infectious process in which the initial or minor nidus is undiscovered or for the origin of which the portal of systemic invasion has eluded detection It is scarcely conceivable that there should be a truly primary endo peri or myocarditis, a fact of fundamental importance that must be a guide in the determination of every regimen directed toward the treatment of cardiac inflammation

For convenience of presentation, the time-honored division of carditis into pericarditis endocarditis and myocarditis may be utilized but let it be emphasized that inasmuch as infection of one layer of the heart is associated almost universally with involvement of one or both of its other mural components such a schema is not to be regarded as an accurate one In just such measure as the infection of one layer or another predominates is the classification warranted and unless it is kept in mind always that the subdivisions are factitious and not entirely true therapeutic procedures may be inadequate

Acute endocarditis has been subdivided by many authorities into a rheumatic or 'rheumatic type" of endocarditis and so-called bacterial or infective type Statistical studies have shown that the former is the predominant one in temperate

zones whereas the nonrheumatic or bacterial variety is the more frequent in tropical and subtropical areas Although the rheumatic variety is probably but a particular form of infectious endocarditis it has such definite characteristics, that it may be justifiable to set it apart from those of different etiology Exclusive of rheumatic endocarditis, Thayer's analysis showed that acute bacterial endocarditis results from infections with various micro-organisms with a frequency that he tabulated as follows

	Per cent
Streptococcus	57
Pneumococcus	14
Staphylococcus aureus	13
Gonococcus	11
Influenza bacillus	4
Staphylococcus albus	1

Acute rheumatic endocarditis is a simple verrucose type leading to the development of a series of small vegetations near the line of closure of the valves, along the chordae tendineae and also on the mural endocardium Although the mitral valve is the site of usual predilection, any of the other valves may be affected and consequent thickening and deformity of the cusps and shortening of the chordae ensues Emboli are rarely set free into the circulation but nearly always myocardial inflammation and less often pericarditis complicates the endocardial disease The other forms of acute bacterial endocarditis cause as a rule larger vegetations which give rise to emboli, more extensive involvement of the endocardium lining the auricles and ventricles and such destructive changes that erosion or rupture of valvular cusps or chordae tendineae occur and mycotic aneurysms of the heart wall, of the aorta or of other arteries may result In them, the coincidence of pericardial involvement is relatively uncommon The deformity of valves and of chordae that result in healed cases gives rise to stenosis or insufficiency at valvular orifices such as occur commonly in rheumatic disease The verrucose endocarditis that occurs as a terminating event in many diseases and the

rare tuberculous endocarditis need no consideration here. The syphilitic involvement of the endocardium that develops when the lesions of aortitis spread to the aortic valves leads to fusion of the cusps with subsequent retraction of the leaflets and to widening of the aortic orifice and aortic regurgitation

In the vegetations of the several types of bacterial endocarditis, exclusive of the rheumatic, the causal micro-organisms are lodged in varying numbers They are found within the deposits and are neither in direct contact with the blood that flows through the chambers of the heart or with that within the vessels that supply the cardiac walls or valves This is a fact of some importance in therapy that seeks the destruction of the invading parasites

The treatment of all forms of acute infective endocarditis, rheumatic and nonrheumatic, is in the main identical There is no specific treatment that has unanimous sanction The recoveries that occur are due chiefly to the resistance of the patient supported by rest, good nursing, proper diet and elimination and by the avoidance of meddlesome treatment. The improvement or cure that follows now and again promptly after the administration of some form of therapy is a chance happening that may give an unearned prestige to a given measure Of first importance is prophylaxis and to accomplish this, proper and adequate treatment of the predisposing or accompanying disease is cardinal Unfortunately, such treatment carried out, however carefully it may be, does not suffice to prevent the development of endocardial involvement, but certain measures are known to be helpful In acute rheumatic fever, recognition of the latency and of the late appearance of signs of endocarditis warrants the continuance of prolonged rest in bed for some days or weeks after all signs of active infection have subsided and demands in the treatment of all forms of local infection the utilization of meticulous surgical technic to minimize chances of dissemination of bacteria and consequent invasion of the endocardium

Of all the therapeutic procedures employed, rest ranks first By means of bodily relaxation, the circulatory rate is slowed

systolic contraction is made more efficient, cardiac nutrition is improved and mechanical trauma of the valves is lessened Sedatives may be required to promote rest but the need for such drugs can be minimized by skilful nursing—a bed well made, a shift of position, the placing of supports such as pillows or pads, the application of cold or of heat to painful areas, well given hydrotherapy, a cleansing bed bath carried out with a minimum of effort by the patient or sponging with tepid or cool water or alcohol, the timely administration of tempting food or drink, avoidance of wearing conversations and other details of care are most important During the active febrile phase of the disease the confinement to bed must be complete —and all unnecessary effort should be avoided Codeine, dionin, morphine, dilaudid, Schlesinger's solution or the nonnarcotic drugs such as chloral, paraldehyde, the barbiturates, etc , may be required and should be administered if needed Now and again when restfulness is due to anoxemia, it is overcome best by placing the patient in an oxygen chamber or tent, a procedure that may be most efficacious in abolishing precordial pain The room or chamber is more satisfactory than the nasal catheter, oral tube or facial mask which cause discomfort and through which it is difficult to get a sufficient concentration of oxygen (50–60 volumes per cent)

Diathermy has been considered useful by some but I have had no experience with it Artificial heliotherapy or exposure to the rays of the sun has a roborant effect and provided it is controlled so as to avoid severe local reactions or any systemic disturbance is an adjuvant to other measures

The diet should contain sufficient calories adequately to maintain nutrition and though high in its content of protein and carbohydrate should be readily digestible and nondistending Liquid and soft foods given at frequent intervals or grouped into five small meals a day are most suitable. No single measure is more beneficial during the febrile stage than an abundance of water the intake of which, however, need not exceed 2 or 3 liters during the twenty-four hours If there are evidences of myocardial strain, the amount ingested

should not be more than 1½ liters Such internal hydrotherapy promotes diuresis and elimination by way of the intestinal tract should be induced by means of enemata, by laxatives or by purgatives To bring about catharsis, the salines and mercurials, especially calomel or blue mass, are the ones of choice though any of the usual preparations may be utilized Inasmuch as strong effort attendant upon the evacuation of the intestines is undesirable and may be hurtful, if there is tendency to strain at stool a suppository or a small enema may be used to start the movement, and in individual cases, a cleansing enema may be given every day or every alternate day

Drugs are of value to afford symptomatic relief but it is more than doubtful if it really helps otherwise successfully to combat the disease In rheumatic endocarditis, salicylates have no prophylactic influence and although there is some electrocardiographic evidence to indicate that they improve the myocardial condition, in our experience when cardiac involvement has developed, they are indicated chiefly for antipyretic and analgesic effects No one preparation has any especial worth, but sodium salicylate, acetylsalicylic acid, phenylsalicylate, etc., are less likely to cause gastric disturbances if they are supplemented by sodium bicarbonate The development of anemia, retarded somewhat by adequate diet and ample sunlight, is treated best with iron Experience in recent years has taught that to secure the desired effect, large doses are needed Blaud's mass, 4 to 6 Gm , or iron and ammonium citrate 3 to 8 Gm in crystals, in capsules or in solution are particularly useful preparations There is seldom need to administer the drug by injection and only if it cannot be taken well by oral administration should the former method be employed

During the last two decades there has been a very general tendency to resort to the intravenous injection of many therapeutic agents and beyond a doubt this procedure is chosen too frequently Were it not that nature is kind, many untoward happenings would be precipitated needlessly and it may not be amiss to state as a preamble to what follows imme

diately, that in our judgment the introduction of foreign substances directly into the circulation should be advised only if it is established that the effect desired cannot be accomplished by oral, intramuscular or subcutaneous administration In many instances when sufficient fluid cannot be taken or retained when given orally, the intravenous injection of glucose is invaluable to combat toxemia, to promote elimination and to supply nutriment Speaking generally, doses of from 200 to 500 cc of a 5 per cent solution are preferable to smaller amounts of greater concentration If there is any tendency to alkalosis, the glucose should be dissolved in normal saline solution, or if an increased intake of fluid alone is indicated, plain normal saline solution suffices

The utilization of various chemotherapeutic agents has its proponents and a great variety of drugs and dyes have been heralded as specifics to promote bacteriostasis, to increase the reaction of the patient against the microbic invader or even to sterilize the blood Mercurochrome, acriflavine, methyl green, gentian violet—to mention only a few—each has its champion Suffice it to say that none has been demonstrated to be truly efficacious except perhaps in cases of bacteriemia without actual endocardial involvement, and then in isolated cases gentian violet and mercurochrome seem to have been of utility when staphylococci were the invasive agents The dose of the latter generally is 0 5 to 1 mg per kilogram of weight given in a 1 per cent solution

Transfusions of whole or of citrated blood supply fluid, hemoglobin and complement, are a stimulant to the formation of blood and may modify the coagulability of it To what extent, if any, they furnish antibodies or accelerate the formation of them is not established In any event, if blood is supplied by transfusion, it is preferable to administer it often in small amounts (200–300 cc) Such repeated transfusions accomplish all that massive ones can and with less attendant danger of precipitating embolism or of inducing cardiac dilatation

The production of "fixation" abscesses, the injection of

foreign proteins, of nucleic acid or of vaccines have no demonstrated value, often cause discomfort and may be actually hurtful So, too, there is no evidence that deep x ray or large doses of vitamin "A" influence the outcome of the disease

How best to deal with foci of infection from which the infection developed is difficult at times to decide If there is a definite nidus of suppuration, adequate drainage of it should be instituted promptly and suitable local measures to eradicate the infection should be employed Operative measures such as the removal of "suspected" teeth or tonsils should be deferred as should any other similar "treatment" the helpfulness of which is not quite patent and when they are carried out the best surgical technic should be observed

Perhaps no phase of the treatment of acute endocarditis is more helpful than is the supervision during convalescence

Limitations of all unnecessary physical and emotional effort are to be insisted upon for a variable number of weeks or months so as to favor the restoration of bodily vigor, to overcome anemia and to secure adjustment of the circulation to what mechanical damage may have been caused by the anatomical changes in the heart and vessels These regulatory measures call for determination of the type of individual concerned as well as a study of his physical status Abundance of sunshine, avoidance of chilling and an abundant, well balanced diet, hasten the restoration to well being and to the resumption of a normal schedule of living. In the case of the rheumatic type of the disease, residence in a tropical area minimizes the risk of a recurrence of active manifestations of the disease

Subacute bacterial endocarditis—endocarditis lenta—requires special comment Due to the Streptococcus viridans (rarely to the gonococcus or to the influenza bacillus) it is productive of destructive pathologic changes that may involve either valvular or mural endocardium or both It is rare for this type of endocarditis to develop in a heart previously normal The important predisposing factors are old rheumatic endocarditis and congenital lesions of the heart and less fre-

quently syphilis and arteriosclerosis It is considered likely that now and again in otherwise normal individuals Streptococcus viridans invades the circulation but that usually it causes no harm, whereas if there has been previous endocardial damage or a congenital malformation is present, endocarditis is likely to develop There is no need here to describe the characteristics of the pathologic changes or of the clinical syndromes produced Suffice it to say that the presence of Streptococcus viridans in a culture of the blood does not of itself establish the diagnosis of subacute bacterial endocarditis even if a chronic valvular disease is demonstrable Such bacteriemia without a fresh involvement of the heart is known to occur and failure to keep the fact in mind has led to erroneous conclusions as to the influence of therapy The condition has a grave prognosis and despite the fact that isolated instances of cure, spontaneous or otherwise, have been reported and although pathologic studies of Libman, Horder and others demonstrate that healing of lesions occurs, I have never seen a proved case of the disease recover The treatment is essentially the same as for acute bacterial endocarditis but if many measures have been tested in the latter, more have been utilized in the former There is no purpose to review them but reference will be made to a few that have the greatest sanction Of the many preparations of arsenic tested, sodium cacodylate is the one of choice partly because of the favorable results reported by Capps, partly because of its tonic effect, partly because it causes no uncomfortable or baneful reactions The dose advocated is from 0 1 to 0 5 Gm intravenously daily Cadman's serum and numerous vaccines and dyes are without proved benefit Small transfusions of the blood of normal people or of those "immunized" with vaccines though at times indicated to relieve symptoms of anemia are not given without the hazard of inducing embolism Whether or not local foci of infection such as infected tonsils, teeth, etc , should be removed when the disease is manifest is still a moot question but wisdom counsels against such procedures It should be emphasized, however, that whenever such potential menaces are eradicated in indi-

viduals who have chronic valvular or congenital heart disease, the most careful surgical technic should be practiced so as to minimize the risk of invasion of the blood stream There are few maladies in which more pressure is brought to bear to "do something" during the long course of illness than in subacute endocarditis Much fortitude is required to refrain from meddlesome therapy and though the family must be treated as well as the patient, nothing should be done that will damage or cause discomfort to the sufferer who cannot be helped

Syphilis of the endocardium is rarely encountered unless one designates as syphilitic endocarditis the downward extension of the reaction of aortitis to the aortic valve This occurs in about one third of the cases of luetic aortitis and results in regurgitation at the aortic ring The choice of the specific measures to be employed in conjunction with the avoidance of strain, of alcohol, of tobacco, etc , is much debated and no one plan is approved universally Some would withhold all antiluetic drugs for fear of weakening walls already damaged, by the too rapid destruction of inflammatory tissue The essential feature of most regimens is the administration of mercury, iodides, arsenicals or preparations of bismuth in moderate amounts over a period of at least two years A useful and safe mode of procedure in the absence of signs of hepatic or renal damage, is to give an initial course of treatment with mercury and iodides The mercury may be given by mouth, by inunction or by intramuscular injections supplemented by moderate doses of potassium iodide over a period of six to eight weeks Then a course of 8 or 10 injections of neoarsphenamine once a week may be administered starting with an initial dose of 0 1 and increasing to a maximum of 0 4 or 0 5 When the administration of arsenic has been completed, the whole procedure may be repeated and the alternation of the two forms of treatment should be repeated throughout a period of two years unless toxic or other untoward symptoms due to the drugs or unless evidences of circulatory weakness develop In many cases, bismuth in the form of iodobismuthite of quinine, or the potassium tartrate salt or preferably the salicylate in oil

0 1 or 0 2 injected intramuscularly may be used in place of either mercury or arsenic or of both Weekly injections should be given supplemented by average doses of potassium iodide The crucial points to be observed are the avoidance of rapid antiluetic action, of systemic reactions and of damage to the liver and the kidneys Carried out with judicious care, such specific treatment is followed by the amelioration of such symptoms as anginal pain, a stay of the progression of structural damage and by prolongation of life (Moore)

Acute pericarditis occurs generally as a manifestation of some other infectious process and is seldom a primary condition so that the treatment of it depends in the main upon the underlying disease The therapy of the dry type and of that with exudation of fluid differs in that in the latter varieties the development of so-called "cardiac tamponade" may require the mechanical relief of pressure or the drainage of a purulent exudate If the fibrinous or serofibrinous inflammation is of rheumatic origin, treatment of the rheumatic fever suffices unless a large accumulation of fluid develops in the pericardial sac In this state, the pericardial fluid is serous and unless it causes a hindrance to efficient cardiac action or to adequate circulatory return, the effusion may be left to absorb spontaneously The salicylates are of value chiefly to lessen pain and to lower the temperature If the pericarditis is due to tuberculosis, pulmonary or disseminated, or if it is a manifestation of a polyserositis, the regimen used in the treatment of tuberculosis generally is indicated In the case of all varieties of acute pericarditis, rest in bed is instituted in conjunction with the measures utilized in any acute febrile illness—namely, an easily assimilable diet of adequte caloric value, an abundance of fluids, regular evacuation of the bowels and sedatives if needed to induce relaxation or sleep To promote comfort and relief from pain, the patient should be permitted to assume the position of choice An ice-cap, hot-water bag or electric pad may be applied to the precordium or drugs such as morphine, codeine, pantopon, dilaudid, dionin, Schlesinger's solution, etc , alone or in combination with salicylates and/or

phenacetin may be administered to relieve pain The latter procedures are preferable to such measures of counterirritation as poultices, blisters, leeches or cupping, all of which have still some vogue

If effusion of any magnitude is formed, signs of tamponade such as dyspnea, cyanosis, distention of the cervical veins, faintness, weak pulse and fall of blood pressure, acute swelling of the liver—paracentesis of the pericardial sac should be carried out promptly Paracentesis of the pericardium is carried out most conveniently by means of a large needle attached to an aspiratory syringe or to a vacuum bottle If the former is the method chosen, a three way attachment to facilitate the discharge of the aspirated fluid may be desirable Under local anesthesia, the needle is made to penetrate the intercostal space indicated by the physical signs in the individual case to offer sure access to the effusion Generally, the site of choice is the fifth left interspace 1 or 2 cc. medial to the lateral margin of flatness as determined by percussion or by the roentgenographic shadow As a rule, this is lateral from the apex or the left border of the heart If fluid is not obtained and the dry tap is not due to obstruction of the needle by fibrin, by thickness of the effusion, or to malposition of the needle, the pericardium may be explored in the fourth or fifth interspace nearer to the sternum or just median to the right border of flatness Occasionally, the needle may be inserted in the epigastrium between the ensiform and the left costal margin or rarely in back in the seventh or eighth interspace in the midscapular line Except in tuberculous pericarditis or in severe rheumatic infections, one tapping of the pericardial sac suffices usually, but it may be repeated at intervals of a few days as often as may be needed If the exudate is purulent, surgical drainage is required To prevent the formation of adhesions, some advocate the introduction of air into the pericardial sac when the tapping is done and if the fluid contains much fibrin it is a procedure of prophylactic value If adhesive mediastinitis or obliterative fibrous pericarditis causes

cardiac embarrassment, surgical measures are required in many cases to lessen the burden imposed upon the heart

Cyanosis and dyspnea not due to cardiac tamponade may be relieved by oxygen Purgatives, ordinary diuretics and limitation of intake of fluid have no real worth to lessen the formation of fluids of inflammatory origin but if the accumulation of pericardial fluid is due to transudation as a result of circulatory failure, the intramuscular or intravenous injection of salyrgan with or without the oral administration of ammonium chloride is a helpful accessory in some cases

Acute myocarditis, in the sense of a true inflammation of the myocardium, is recognized rarely at the bedside It is met with clinically chiefly in rheumatic fever, occasionally as a complication of diphtheria or of pyemia, very rarely in syphilis of the cardiovascular system and in other infectious diseases such as typhoid fever, etc Were it not for the knowledge gleaned in the pathologic laboratory, the development of true myocarditis would not be suspected in many cases in which the existence of it is sought for because of the established incidence of its occurrence as a manifestation of systemic infections Moreover, electrocardiography has shown evidences of myocardial involvement when manifestations of intramural cardiac disease were not detected by other means Generally, the condition will be overlooked unless the myocardium fails adequately to maintain the circulation during the course of an infectious disease Presumptive signs are a disproportionate, persistent tachycardia, the sudden development of heart block, acute dilatation of the heart in the absence of valvular disease, involvement of the coronary arteries or of hypertension, or unless electrocardiographic tracings show the changes associated with alteration of myocardial function that cannot be attributed to drugs such as digitalis

As in acute endocarditis, the first therapeutic consideration is the proper treatment of the infectious process responsible for the development of the myocardial disease Except in the cases of diphtheria, of rheumatic fever and of syphilis, there is no specific medication, but those rules observed generally in the

management of a systemic infection are to be carried out Rest, adequate hydrotherapy and dietary regulation, promotion of elimination and the amelioration of subjective disturbances such as pain, sleeplessness, delirium, etc , each calls for the measures efficacious ordinarily to secure them In diphtheria, an early diagnosis and the immediate administration of adequate doses of antidiphtheric serum are the best procedures to prevent the development of a myocardial complication and combined with rest, prolonged sufficiently, insure protection of the heart from serious damage.

Whether or not cardiac damage can be prevented entirely in individual cases of rheumatic fever is still an undecided question The universality with which alteration of the conduction time is demonstrable by electrocardiographic studies in active rheumatic disease seems to indicate the development of at least some disturbance of the myocardium in practically all cases The efficacy of salicylates to prevent cardiac involvement is doubtful to say the least and no reliable evidence substantiates the statements of such prophylactic action To what extent they may be useful to minimize myocardial damage or to help rectify such as has developed there is some difference of opinion inasmuch as some data derived from electrocardiography indicate such beneficial influence In any event, derivatives of salicylic acid should be administered for their antipyretic and analgesic effects

The indications for the administration of digitalis and drugs with like action are likewise the source of much discussion It has been shown that digitalis decreases the size but lessens the volume of output of the normal heart, whereas it causes a decrease of the size but causes an increase of the minute volume output of a damaged heart. So long as the myocardial damage does not impair the cardiac function, foxglove is not called for If there is evidence of dilatation of the heart or of circulatory failure present or impending, digitalis should be administered whether or not the rhythm is altered and whether or not heart block is present. Convincing evidence is at hand to show that although foxglove and derivatives of it have no

capacity to lessen tachycardia if the myocardium is normal, such drugs have often their usual influence upon the rate and the efficiency of a heart that is rapid because of myocardial damage In my experience, the drug has relatively less value in acute febrile states for the general toxic manifestations are frequently induced by it before an influence is exerted on the circulatory apparatus In what form and by what route it is best to give digitalis have provoked much thought The many and varied preparations of the drug are reminders of a time when a reliably standardized, potent tincture or powdered leaf was difficult to obtain and the enthusiasm for the administration of digitalis by injection intramuscularly or even intravenously recalls the days when it was not considered practicable rapidly to digitalize a patient by the oral route and when the central origin of emesis caused by the toxic action of the drug was overlooked Now that the standardization of digitalis in terms of cat units is practiced generally, potent standardized preparations are available and the dose of the drug required for effective action can be calculated accurately in terms of body weight of the patient The rapidity with which the digitalization of the individual is to be accomplished can be varied by the administration of larger or smaller fractions of the calculated total at intervals of four or more hours Because of this, the hypodermic injection of digitalis is required no longer except in those instances in which coma or cerebral disturbances such as delirium, vomiting or dysphagia, prevent the ingestion of the drug or in which the condition of the gastro-intestinal tract precludes adequate absorption from it For administration by mouth, a good powdered leaf or a potent tincture is to be chosen and for injection any of many reliable products such as digifolin, digalen, etc , is satisfactory

Just as complete, prolonged rest, proper diet, adequate elimination, hydrotherapy, meticulous care of mouth and skin, sedatives to promote relaxation and analgesics for pain are required during any acute infectious disease, so are they indicated in the one under discussion If there are evidences of insufficient aeration of the blood, the resultant anoxemia mani-

fested by altered respiration and cyanosis is to be treated by the administration of oxygen Breathing in an atmosphere that contains 40–60 volumes per cent of that gas not only increases the oxygen saturation of the blood, relieves dyspnea, overcomes cyanosis and precordial pain but frequently lessens or abolishes restlessness or delirium, induces relaxation or sleep, improves the quality of the pulse and the efficiency of the circulation If adequate amounts of fluid cannot be taken by mouth or if taken it is not retained, fluids may be given intravenously, subcutaneously or rectally Physiologic solutions of sodium chloride, or solutions of glucose in water or in saline solutions administered by one or more of these routes are helpful to prevent or to overcome dehydration of the tissues, to maintain circulatory volume and to improve elimination by the kidneys There are few conditions in which the administration of glucose is of more value than in those in which there is inflammation or anoxemia of the myocardium Although some prefer concentrations of glucose as high as 10 or 20 per cent, it is our judgment that 5 per cent is to be chosen as a rule Frequent injections, once or twice daily, made slowly and at body temperature are attended by less strain on the heart than are the administration of larger amounts For the same reason, repeated small transfusions (250–350 cc) of whole or of citrated blood are to be preferred to one or more transfusions of 500 to 1000 cc. Needless to say, the proper typing and matching of blood cells and serum and serologic study (Wassermann reaction) of the donor must be made before blood is injected into a patient.

Of the many forms of hydrotherapy available, sponging is the one to be preferred in the treatment of the several forms of febrile cardiac disease. The procedure unless carried out skilfully will have a baneful effect because of the physical effort imposed upon the patient and the shock to his nervous system Given as it should be without any active exertion by the recipient and after a reassuring talk as to what the procedure means and what it will accomplish, a sponge bath of tepid or cool water, of alcohol and water or alcohol alone will act as a

stimulant to respiration and circulation, will cleanse the skin, promote elimination, quiet delirium and lower the temperature If the patient is very "toxic"—mentally dull or delirious—symptoms of intoxication will often be lessened at least temporarily and food will be taken more readily Such hydrotherapy is often one of the best of therapeutic agents and may be repeated at four hourly intervals throughout the day so long as conditions demand Other forms of stimulation are called for now and again and many different drugs have enthusiastic proponents—strychnine has little if any worth as a circulatory stimulant in these cases—alcoholic drinks do no more than supply a source of calories—caffeine in one form or another, especially the sodiobenzoate or the citrate, may help tide over an episode of circulatory weakness with depression of urinary excretion, but these preparations are to be used sparingly if there is active delirium, camphor and its derivatives have only a very evanescent action and, in our experience, coramin is without definite effect, epinephrine may be given subcutaneously, intravenously or may even be injected into the heart in acute circulatory collapse but is to be avoided if there have been attacks of anginal character The xanthine diuretics, especially theophylline diethylene amine (0 1 Gm twice or three times a day), are indicated if there is reason to believe that an insufficient supply of blood is reaching the myocardium because of the spasm of the coronary arteries or if there is edema of the tissues Should evidences develop of failure of the right chambers of the heart (cyanosis, distention of the cervical veins, a regurgitant pulsation of the jugular veins, acute swelling of the liver, peripheral edema, etc), a venesection with the removal of 200–500 cc of blood may be lifesaving, provided anemia does not contraindicate this measure In addition, as in all cases in which there are signs of congestive heart failure, prompt digitalization should be brought about and adequate amounts of morphine and of atropine should be administered

Once the acute phase of cardiac infection has passed and the period of convalescence is initiated, new problems present

themselves The after-care of those who have weathered the storm of acute carditis requires meticulous attention to details, avoidance of all excesses, "moderation in all things" No less important than the physical status of the convalescent cardiac are his mental attitude and his psychic balance Physical rest for weeks or months to help restore circulatory efficiency and reserve, ample nourishment and hematinics such as iron (ferric ammonium citrate, 6 Gm , or iron subcarbonate, 3–6 Gm , etc.), residence in a warm, equable climate with abundance of sun light, natural or artificial, carefully graduated exercise when physical activity is resumed, with care to rest before fatigue is induced, avoidance of chilling and of acute infections, removal of evident foci of local infection with the best of surgical technic, all are factors or cardinal utility to restore and to main tain health But none of these transcends the importance of restoring or of preserving emotional balance and a proper in sight It is imperative that the patient learn to follow a path between a clear understanding of his physical status and a miserable hypochondriasis, between a needed restriction of bodily and nervous activities and an unwarranted degree of invalidism, between a rash optimism and a painful depression To guide the convalescent in the middle way he should go calls for a real understanding of human nature and for an acquired knowledge of the mental and emotional constitution of the individual that will lead to an ordered way of living and make for a restoration to well being and to a capacity for action unattainable by other means

In brief 1 Acute inflammation of the heart is rarely if ever a primary disease but is a manifestation of a systemic in fection

2 The aim of treatment should be to overcome the under lying cause of the cardiac infection to relieve symptoms and to prevent complications

3 At this time there is no known specific therapy avail able and until such is found for any of the many varieties of infection encountered reliance must be placed upon accurate diagnosis good nursing measures directed toward the relief

of symptoms and an assiduous avoidance of procedures that may be hurtful

4 Good judgment is needed so as not to abandon old and tested methods in favor of new ones that have novelty only to recommend them and at the same time there should be no unwillingness to test new remedies for fear they may not be efficacious or because of the effort required to master a new technic

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR WILLIAM S LOVE, JR

UNIVERSITY OF MARYLAND

TREATMENT OF SYPHILIS OF THE HEART AND OF THE CORONARY ARTERIES

THE subject of the treatment of cardiac syphilis has been a controversial one for many years In the earlier days of arsphenamine treatment, cardiac patients were subjected to the same general routine as other syphilitics It soon became obvious that this was a dangerous procedure, many instances of sudden death or rapidly progressive heart failure resulting The cause of these unfortunate accidents has been shown to lie in one of three types of reaction, namely

1 Therapeutic shock (Herxheimer reaction) in which sudden death occurs in from twenty four to forty eight hours after the administration of arsphenamine

2 Intrinsic arsphenamine toxicity Here there is a predisposition to the development of ventricular tachycardia and fibrillation in the already injured heart [1]

3 The therapeutic paradox This series of events has been emphasized by Wile,[2] and consists of an immediate general improvement subsequent to arsenical treatment, followed by a rapid deterioration and increase in the original defect. Wile has suggested that this type of reaction may be due to too rapid replacement of the syphilitic products by scar tissue or that their rapid disintegration has produced a chemical change deleterious in effect upon the local lesion

Nitritoid reactions also may occur, and are indeed alarming both to the patient and to the physician, but rarely result fatally

The frequency of the above-mentioned disastrous results of arsphenamine treatment of patients with syphilitic heart disease eventually led to practically the abandonment of this mode of therapy for a period of years During this time some writers advocated that no specific therapy be administered to such patients, and relied upon rest, general hygienic measures and digitalis Others recommended potassium iodide, still others potassium iodide and mercury More recently there has been a recrudescence of interest in the arsphenamine treatment of syphilis of the heart and an increasing number of writers is reporting its use It seems probable that the most important factors in the use of the arsenicals are the proper selection of the preparation to be used, and the amount given At the outset of this discussion I believe I should state that salvarsan (early 606) should never be used in the treatment of syphilis of the heart Neoarsphenamine is the preparation used in this clinic, and the initial dosage is not greater than 0 1 or 0 2 Gm

THE VALUE OF NEOARSPHENAMINE AS A THERAPEUTIC AGENT IN THE TREATMENT OF SYPHILIS OF THE HEART

In evaluating a therapeutic procedure it seems obvious that the points to be considered are whether the said procedure relieves symptoms, increases the duration of life, cures the disease, and is not too hazardous to permit of its application

1 **Effect of Neoarsphenamine upon Symptoms of Patients with Syphilis of the Heart**—It is generally conceded that the cardiac syphilitics treated with neoarsphenamine have a considerable symptomatic improvement For example, Hines and Carr[3] found relief or improvement in 25 of 44 instances of cardiac pain, 28 of 48 of dyspnea, 13 of 24 of palpitation, 9 of 17 cases of edema, etc , summarizing their findings in the statement that symptomatic improvement is believed to be a neoarsphenamine effect in 57 per cent of their cases We have had a similar experience and indeed it is often difficult to have patients continue treatment because of their rapid symptomatic improvement

2 **Increased Duration of Life of Patients Treated with Neoarsphenamine**—It is difficult to find satisfactory statistics upon which to append a decision in regard to this point It is my decided impression that such treatment does prolong life, and the figures upon which I base this conclusion will be presented in the statistical review of the cases treated at the University Hospital Moore and Danglade[4] contrast 25 patients with aortic insufficiency who were given no anti syphilitic treatment and who lived an average of thirty two months after the onset of symptoms (twenty were dead at the time of publication) with 20 patients who received more than a year of treatment and who lived an average of sixty five months after the onset of symptoms and were all still living at the time their observations were reported Cotton[5] reported 58 treated cases of cardiovascular syphilis in whom the death rate was 9 8 per cent lower than that of a similar untreated group, over a five-year period Reid[6] states that the average duration of life in a group of patients with little or no treat ment was one year, in a group with moderate treatment three years He further states that of those with early and prolonged treatment many were able to go back to full physical work, and life was prolonged

3 **The Cure of Syphilis of the Heart**—It would seem self-evident that permanent structural alterations in the heart will not be removed by the administration of neoarsphenamine However, arrest of the active foci may be hoped for I have seen 2 cases in which aortic diastolic murmurs disappeared under treatment, but it must be kept in mind that such murmurs may be due to dilatation of the aortic ring and not to an actual valvular involvement Two cases of partial heart block showed no improvement in auriculoventricular conduction following treatment There is fairly frequently a diminution in the in tensity of the Wassermann reaction, 29 of 48 patients so fol lowed showing this effect of treatment In only three, how ever, did the Wassermann become negative Hines and Carr[3] report that out of 85 patients the Wassermann became nega tive in 23, less strongly positive in 3, and remained unaffla

enced in 62 (I assume that there is some minor typographical error in these figures)

4 **Hazards of Neoarsphenamine Therapy in Syphilis of the Heart**—With the use of the proper dosage, neoarsphenamine treatment does not seem sufficiently hazardous to be interdicted in cases of syphilis of the heart In their report Hines and Carr[8] noted that 10 of the 85 patients became symptomatically worse, but that no cases of sudden death or aneurysmal rupture occurred In the 60 cases to be analyzed in this study there was no instance of death directly attributable to treatment Two patients with aortic insufficiency receiving respectively three injections of 0 2 Gm and two of 0 2 Gm of neoarsphenamine died within three months The first, with severe substernal pain and collapse, the second with rapidly progressive heart failure This last patient had complained of anginal pain, which had been so relieved after the second treatment that he did not again report until after the onset of failure These 2 cases may represent the therapeutic paradox However, Pincoffs and Love[7] have recently emphasized the syndrome of coronary ostial stenosis in syphilitic aortitis, pointing out the rapidly progressive downhill course of such patients, and the high incidence of angina pectoris as a symptom of this lesion The first of the above-mentioned patients came to autopsy and such a lesion was found It seems possible that the rapid progression of some cases with or without treatment may be ascribed to the presence of such ostial stenosis Several patients have had nitritoid reactions without fatal outcome Under these circumstances, however, neoarsphenamine has been temporarily discontinued Several patients have complained of burning retrosternal discomfort This symptom disappeared when the dosage was diminished

TECHNIC OF TREATMENT

The technic developed in treating patients with cardiac syphilis must be elastic, and one that is not dogmatically adhered to The appearance of any untoward symptoms or reactions should be considered a definite indication to alter the pro-

cedure being followed Under such circumstances we have either reduced the dosage of neoarsphenamine or discontinued it temporarily These patients are handled conjointly by the Heart and the Syphilis Clinics of the University Hospital I wish to express my thanks to Dr Harry M Robinson, Chief of the Syphilis Clinic, for his hearty and helpful cooperation in this work The technic then that we have developed is as follows

1 **Aortitis without Aortic Insufficiency, Heart Failure, or Angina Pectoris**—This group does not properly fall into this discussion, since I have included no cases without evidence of cardiac dysfunction However, since the usually accepted physical signs of aortitis may be the only ones demonstrable in the neighborhood of the heart even when more striking symptoms are present, the treatment of this condition is included, and serves as a basis for further elaboration Such patients are routinely started on 0 1 Gm neoarsphenamine intravenously and given eight to ten such treatments at weekly intervals This course of neoarsphenamine is then followed by a like number of intramuscular injections of bismuth These two procedures are then followed alternately, the dosage of neoarsphenamine never exceeding 0 6 Gm and frequently not over 0 4 Gm No rest periods are given until a year of treatment has been accomplished, unless symptomatically indicated, when potassium iodide and mercury are then given by mouth

2 **Asymptomatic Aortic Insufficiency**—Patients with this lesion are treated in a similar fashion to the first group with the exception that the dosage of neoarsphenamine is increased much more gradually, and 0 4 Gm is the maximum amount given

3 **Congestive Heart Failure**—Patients in this functional state are hospitalized, where the usual appropriate measures are undertaken to restore compensation When this has been accomplished, and the patients are ambulatory, they are then given 0 1 Gm neoarsphenamine at weekly intervals for two weeks Treatment is then continued in the out patient department as outlined above In this group, however, the dosage of

neoarsphenamine given rarely exceeds 0 2 Gm In this group of patients we continue digitalis in the dispensary in daily dosage varying from 1½ to 3 grains or more as their condition may indicate, with rest periods of a week every four to six weeks It is a distinct clinical impression that such patients do better taking digitalis rather constantly, but an impression for which I have no statistical evidence Some of the theobromine derivatives have also proved useful in maintaining compensation [8]

4 **Angina Pectoris and Suspected Coronary Disease** —Patients with a definite anginal syndrome are hospitalized when possible They are first given an ascending dosage of potassium iodide, reaching a maximum of 60 grains three times daily in ten days The procedure in regard to bismuth and neoarsphenamine is then reversed, the patient receiving bismuth first, and then neoarsphenamine The dosage of the latter does not exceed 0 2 Gm It is in this group of patients that coronary ostial stenosis or other coronary involvement is most common Many writers deplore the use of any arsenical where coronary disease is suspected We have not observed untoward results subsequent to the treatment outlined where this diagnosis has been suspected Where initial hospitalization has not been possible, the patient has been ordered to discontinue all work and remain at home in bed during the early phase of treatment Several patients have been given neoarsphenamine in 0 1-Gm doses without initial preparation with potassium iodide and a heavy metal, but, even though disaster did not follow, this procedure is not recommended Theobromine derivatives have often proved of value to relieve pain in these patients

RESULTS OF TREATMENT

Table 1 lists the total cases observed and the data available in regard to the results of treatment expressed in terms of duration of life We have found it difficult to follow adequately many of our patients Fifty-two of the 60 patients were of the Negro race, and in Baltimore members of this race are constantly moving from place to place or leaving the city

TABLE 1

EFFECT OF NEOARSPHENAMINE THERAPY EXPRESSED IN DURATION OF LIFE, UPON 60 CASES OF SYPHILIS OF THE HEART

Treatment	No. of cases.	Status at End of 1 year L. D	2 yrs. L. D	3 yrs. L. D	4 yrs. L. D	5 yrs. L. D	6 yrs. L. D	7 yrs. L. D
None	8	? 7						
Less than one course	8	2 5	? 1					
One course	8	5 3	1 1	?				
Less than one year	5	4 ?	3 ?	2 1	?			
One year	8	8 0	4 ?	3 ?	1 1	?		
Two years.	15	15 0	15 0	8 ?	2 ?	1 ?	1	1
Three years or more	8	8 0	8 0	8 0	6 ?	5 ?	4 ?	4
Total	60							

However, every effort has been made to follow them Many patients listed as having been followed two or more years are still continuing under treatment at the end of the period noted Of those patients with less than one course of neoarsphenamine, 8 received no treatment at all Of these 8, 7 were followed to the time of their death and lived an average of eight months They were not treated because of refusal to accept such treatment or because of hospitalization elsewhere and failure to return to this clinic. One patient died suddenly before hospitalization could be arranged

Table 2 lists 12 cases of aortitis uncomplicated by aortic insufficiency No patients are included in this group who did

TABLE 2

EFFECT OF NEOARSPHENAMINE THERAPY EXPRESSED IN DURATION OF LIFE, UPON 12 CASES OF AORTITIS WITH EVIDENCE OF HEART INVOLVEMENT

Treatment	No. of cases.	Status at End of 1 year L. D	2 yrs. L. D	3 yrs. L. D	4 yrs. L. D	5 yrs. L. D	6 yrs. L. D	7 yrs. L. D
One course	2	2 0	?					
One year	2	2 0	?					
Two years	4	4 0	4 0	4 0	1 ?	1	1	1
Three years or more	4	4 0	4 0	4 0	3 ?	2	2	2
Total	12							

not have evidences of cardiac dysfunction Patients with congestive heart failure have not been included where there have been obvious other etiologic factors such as hypertension or clinical arteriosclerosis In this group there are 3 patients who suffered with angina pectoris, of whom all recovered symptomatically Two were followed for two years and 1 for four years, all being symptom-free and in good condition at the last visit One patient had angina pectoris and also a moderate degree of congestive heart failure He was followed for one year and was symptom-free at that time Two more patients had congestive heart failure, 1 being followed one year and 1 three years, both being symptom-free at the time of their last visit A question may be raised in regard to what led to the congestive failure and angina in these patients without aortic insufficiency Pincoffs and Love[7] have pointed out the frequency of angina pectoris as a symptom of coronary ostial stenosis and they have also shown that congestive heart failure may result from this lesion Love and Warner[9] have reported the frequency of myocardial fibrosis as a result of ostial occlusion or stenosis and also the frequency of sclerosis of the smaller coronary radicles in syphilitic heart disease It is probably upon the presence of such lesions as these, that the symptomatology above discussed, depends Extensive active syphilitic myocarditis may occur but I know of no way to recognize this lesion, and moreover, I have not seen it at autopsy Further discussion of coronary lesions will occur in conjunction with Table 4

Table 3 comprises 48 cases of aortic insufficiency and shows their response to varying amounts of neoarsphenamine treatment Of these 48 cases 19 were in some degree of heart failure before treatment started Eight of the 19 fall in the group with no treatment or less than one course of neoarsphenamine, 3 in that with one course only, 1 in that with less than one year of treatment, 5 in that with two years' treatment and 2 in the group with three years or more of treatment I have no fair statistics upon which to base a conclusion as to whether neoarsphenamine treatment prolongs life when such

TABLE 3

EFFECT OF NEOARSPHENAMINE THERAPY EXPRESSED IN DURATION OF LIFE, UPON 48 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

		Status at End of													
Treatment.	No. of cases.	1 year		2 yrs.		3 yrs.		4 yrs.		5 yrs.		6 yrs.		7 yrs.	
		L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
None	8	?	?												
Less than one course	8	2	5	?	1										
One course	6	3	3	1	1	?									
Less than one year	5	4	?	3	?	2	1	?							
One year	6	6	0	4	?	3	?	1	1	?					
Two years	11	11	0	11	0	4	1	1	?	?					
Three years or more	1	4	0	4	0	4	0	3		3		2	?	2	
Total	48														

treatment is started after the patient has already developed heart failure. I believe, however, that there is every indication in the table and discussion that it does

TABLE 4

EFFECT OF NEOARSPHENAMINE THERAPY EXPRESSED IN DURATION OF LIFE UPON 12 CASES OF SYPHILITIC HEART DISEASE WITH ANGINA PECTORIS (SUSPECTED CORONARY DISEASE)

		Status at End of									
Treatment	No. of cases.	1 year		2 yrs.		3 yrs.		4 yrs.		5 yrs.	
		L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
None	5	0	5								
Less than one course	1	0	1								
Less than one year	1	1	0	1	0	1	0	?			
One year	1	1	0	?							
Two years	3	3	0	3	0	1	?	1		?	
Three years or more	1	1	0	1	0	1	0	1	0	?	
Total	12										

Table 4 comprises 12 cases presenting angina pectoris as a prominent symptom. Lamb[10] has commented that in his cases all patients presenting this symptom have shown some type of involvement of the coronary arteries, ostial occlusion and simple coronary arteriosclerosis accounting for most. Pincoffs

and Love[7] reported that 86 6 per cent of their autopsied cases of ostial occlusion presented this symptom It seems permissible to strongly suspect ostial stenosis in those patients forty-five or under with syphilis of the root of the aorta, who present this symptom and in whom there does not exist hypertension or obvious arteriosclerosis Of the 12 patients in Table 4, 4 were forty or under, and 2 were forty-two, 2 forty-three, and 2 forty-five Eight of these patients were examined electrocardiographically and coronary T-waves were present in 4 Justin and Pardee[11] reported 85 per cent of patients with syphilitic aortic insufficiency to have abnormal T-waves, and that 20 per cent showed the coronary type They conclude that T-wave changes in the electrocardiogram of patients with syphilitic aortic insufficiency should be viewed as an indication of serious coronary involvement

Of these 12 patients with angina as a symptom, 3 had aortitis without aortic insufficiency No electrocardiographic changes were noted in 2 of these 3 patients, the third was not so examined All 3 of these patients were living, symptom-free at the time of the last observation made upon them, which was in 2 cases two years, and in the third four years after the initiation of treatment

The other 9 patients in this group had aortic insufficiency as well as angina pectoris Six of these were examined electrocardiographically and 4 showed coronary T-waves Of the 4 with T-wave changes, 3 died within one year One suddenly before treatment could be instituted, and 2 in other hospitals during the course of the year These also had received no treatment One patient with inversion of the T-waves in leads I and II received potassium iodide, then a course of 8 intravenous injections of 0 1 Gm of neoarsphenamine He then received a similar course of bismuth followed by a second series of neoarsphenamine injections, in which the dosage was 0 2 Gm This patient recovered symptomatically He could not be traced during the next three years, and then returned to the dispensary saying he was living in another state, was working and symptom-free He had received an uncertain number of

injections from a private physician, and of course did not know what they were He was to return for another electrocardiogram, but failed to do so and could not be traced

I believe the evidence at hand indicates that the prognosis of these patients with angina pectoris is indeed grave In an unpublished study[1] made some years ago, I found that the average duration of life in cases of syphilitic heart disease with this symptom was seven months as contrasted with about eighteen months in cases in which it was not present I now believe that the poor outlook for such patients is because the vast majority of them have developed such coronary lesions as ostial occlusion or widespread endarteritis of the smaller branches of the coronary system The ostial lesions are particularly prone to occur in those cases with aortic insufficiency, because in these the aorta is already involved by the syphilitic process in the immediate vicinity of the coronary orifices Experience does not suggest that treatment, when such lesions have fully developed, will resolve the resulting fibrosis and stenosis of the proximal portion of the coronary arteries However, if the process has not gone too far, it may be inhibited from further progression in a status still compatible with life Treatment, of course, should be instituted before such lesions have occurred, and this is but another reason for the persistent treatment of syphilitic aortitis and aortic insufficiency Some few cases may give such worthwhile response to neoarsphenamine treatment as that quoted above, and others where the diagnosis is not yet certain, may have their lives considerably prolonged The risk attached to neoarsphenamine therapy of these patients seems to add but little to the precariousness of their already existing state

SUMMARY

A general outline for the treatment of patients suffering with various forms of syphilis of the heart has been given Evidence has been adduced to indicate that such treatment is worthwhile Even in the suspected presence of coronary disease the use of neoarsphenamine is advocated because the

prognosis in these cases is extremely grave when untreated, and evidence has been offered to suggest that considerable prolongation of life and symptomatic relief may be obtained with such treatment It is suggested that certain cases which might be illustrative of the therapeutic paradox are perhaps in reality associated with coronary ostial occlusion

BIBLIOGRAPHY

1 Reid, W D The Mechanism of the Toxic Action of Arsphenamine on the Heart, Jour Amer Med Assoc, 84 883, 1925

2 Wile, U J The Treatment of the Syphilitic Liver and Heart A Therapeutic Paradox, Amer Jour Med Sci, 164 415, 1922

3 Hines, L E, and Carr, J G The Use of Intravenous Arsenicals in the Treatment of Cardiovascular Syphilis, Amer Heart Jour, 6 142, 1930

4 Moore, J E, and Danglade, J H The Treatment of Cardiovascular Syphilis, Amer Heart Jour, 6 148, 1930

5 Cotton, T F Cardio-aortic Syphilis and Its Treatment, Brit Med Jour, 1 855, 926

6 Reid, W D Discussion, Amer Heart Jour, 6 155, 1930

7 Pincoffs, M C, and Love, W S, Jr Observations upon Syphilis of the Heart, Coronary Ostia, and Coronary Arteries I With Special Reference to the Clinical Picture Presented by Syphilitic Stenosis of the Coronary Ostia, Amer Jour of Syph and Neur, 18 145, 1934

8 Love, W S, Jr A Clinical Survey of the Action of Theocalcin, Bull of the School of Medicine, Univ of Maryland, January, 1930

9 Love, W S, Jr, and Warner, C G Observations upon Syphilis of the Heart, Coronary Ostia, and Coronary Arteries II With Special Reference to the Myocardial Lesions Noted in Stenosis of the Coronary Ostia, Amer Jour of Syph and Neur, 18 154, 1934

10 Lamb, A R, and Turner, K B Cardiovascular Syphilis, Nelson's Loose Leaf Medicine, 4

11 Justin, I R, and Pardee, H E B Abnormal Electro-cardiograms in Patients with Syphilitic Aortitis (Summary), Amer Heart Jour, 6 162, 1930

12 Love, W S, Jr The Occurrence and Significance of Angina Pectoris as a Symptom of Luetic Aortitis, read before the annual meeting of the Medical and Chirurgical Faculty of Maryland 1927

Medical Clinics of North America
May 1935 Baltimore Number

CONTRIBUTION BY DR E W BRIDGMAN

THE JOHNS HOPKINS UNIVERSITY

THE TREATMENT OF THE DIFFERENT FORMS OF THE IRREGULARITY OF THE HEART (CARDIAC ARRHYTHMIAS)

IN this symposium on "The Treatment of Heart Disease," I have been assigned "The Treatment of the Cardiac Arrhythmias"—a subject having connotations that must be made clear before there can be intelligent discussion Perhaps the difficulty can be more readily appreciated if I suggest the confusion that would arise in your minds were you asked to discuss the treatment of jaundice! Here is a disorder, as you know, which may be the result of many and various pathologic dysfunctions, involving different organs of the body besides the liver What an involved discussion would ensue! You will agree that it would be important to emphasize that jaundice is a symptom, not a disease, and to take up the various diseases that might include jaundice as a symptom Until a correct diagnosis has been made, and the organ or system of the body involved has been determined, the treatment of jaundice as such is impossible

In the same way, none of the different types of cardiac arrhythmias are clinical entities They are symptoms that may point to dysfunction, pathologic or physiologic, of organs outside of the cardiovascular system, as well as to abnormalities in the heart beat Indeed, certain arrhythmias have existed in individuals whose hearts, according to study during life and from subsequent pathologic investigation, have been quite normal Again, the presence of certain of the arrhythmias, far from being indicative of cardiac disorder, is prognostically important because it suggests that the heart has not been affected

during the course of a disease that sometimes involves the heart—a fact long since noted by the pioneer of all study on cardiac arrhythmias—Sir James Mackenzie

Again, most of the arrhythmias may develop as transitory phenomena during the course of various infectious fevers It is quite common, for instance, to discover precocious systoles, auricular fibrillation, or even heart block in a patient during the course of an attack of pneumonia, and to find that these irregularities disappear during convalescence Many such patients have been examined clinically years afterward, and no evidence has been found of cardiac disease, occasionally, individual patients with the same transitory findings have come to autopsy years later, and nothing unusual could be made out in their cardiovascular system

There are various extracardiac conditions that may be associated with cardiac arrhythmia Thus, gastric or rectal distention may lead to precocious systoles When one considers the thin diaphragmatic musculature that separates the heart from the abdominal organs, it is not difficult to understand that simple mechanical irritation of the heart is possible, and —quite like touching the heart during thoracic operations— apt to produce ectopic contractions Such a conception has been repeatedly confirmed by the injection of air under a little pressure into the stomach or rectum of experimental animals— precocious systoles can be produced There are many high-strung individuals who, under the stress of fatigue or anxiety, may develop precocious systoles or attacks of paroxysmal tachycardia, and yet their hearts may show no evidence of disease, even during a long life Moreover, the ingestion of certain chemicals—coffee, tobacco, alcohol, and certain foods— may be followed by paroxysms of precocious systoles, and yet observation of the heart during succeeding years may reveal no evidence of heart disease The dosage necessary is extremely variable, suggesting that there is a great variation in the sensitivity of individuals

It is evident, then, that the cardiac arrhythmias are not necessarily significant of actual heart disease, and that the dif-

ferent forms of irregularity of the heart should be considered as symptoms of some underlying disorder, that may or may not originate in the cardiovascular system This fact allows me to emphasize the impossibility of treating one organ as if it had no relation to the rest of the body It is the constant pitfall of so-called "medical specialists" and suggests the danger, especially in teaching hospitals, of subdividing the medical clinic into cardiac, gastro-intestinal clinics, and so forth

Granted, then, that our subject today comprises those arrhythmias that have to do with heart disease, and that care ful study has eliminated disorders of other systems, it is rela tively simple to outline a classification of the arrhythmias, and to discuss the treatment of, at least, the commoner types of irregularity of the heart It should be understood that there is no space in this discussion for the clinical differentiation of the arrhythmias or for the interesting study of the mechanism of their production Those of you who want to review these sub jects would find it profitable to read Dr Thomas Lewis's books on "The Clinical Disorders of the Heart Beat," and "The Mechanism of the Heart Beat"

SINUS ARRHYTHMIA

For purposes of discussion, I will group under this heading vagotonia, sympathicotonia, respiratory and youthful arrhyth mias, and sino-auricular block This last irregularity of the heart beat does not definitely belong to the simple arrhythmias, although most writers regard it as a vagal phenomenon It is occasionally seen in the presence of other findings that suggest cardiac damage, but much more frequently it is to be found in patients during early adult life, to disappear with the advance of age I have followed several such cases for many years, and although I have, personally, never seen autopsies on patients with this disorder, cardiac studies have revealed no evidence of heart disease ten and fifteen years after the disappearance of the arrhythmia. Moreover, autopsies on similar cases have been reported in the medical literature where no evidence of cardiac disease was discovered

By sympathicotonia is meant a body make-up with evidence of increased stimulation of the sympathetic system The accompanying tachycardia characterizes a general abnormal state without evidence of actual cardiac disease, except for rare instances Hyperthyroidism is the striking example, and here one is concerned with the thyroid as the organ for study, of course, a persistent toxemia of thyroid origin commonly leads to cardiac damage The hyperthyroidism found in early hypertensive cardiovascular disease is obviously of different significance, although here, too, cardiac disease eventually develops Before one is satisfied with the diagnosis of the functional disorder, sympathicotonia, where tachycardia is the presenting symptom, it is well to rule out the possibility of a generalized disease, such as early tuberculosis Individuals sensitive to caffeine or tobacco may have symptoms of sympathicotonia, even following the use of small amounts of these chemicals Abstinence from their use is the treatment Effort syndrome, where one is concerned, generally, with increased sympathetic activity associated with delayed convalescence, anxiety or fear psychoses, should be mentioned Here the treatment lies in the use of graduated exercises, bromides and reassurance Remarkable cures are often possible, with persistent care and interest by the physician

In the same way vagotonia represents an overactive vagus without, commonly, any disease of the heart Hyperacidity, spastic colon, and a slow pulse are symptoms not of a cardiac disease, but of an increased vagal activity that overbalances the sympathetic system Pulse rates as low as forty to fifty may be found Obviously, disease of the heart must be ruled out, because such slow rates bring up the possibility of heart block But if there is no clinical evidence of heart disease—cardiac enlargement or cardiac insufficiency—and if the electrocardiogram is normal, and shows an increased rate following exercise, the physician is quite safe in disregarding the cardiovascular system, treating the underlying disorder of the nervous system The use of belladonna to the point of saturation is indicated, and, not infrequently, relief is not ob-

tained until as much as a drachm of the tincture is used three times daily Vagal bradycardia is often found during the convalescence from infectious fevers, it is sometimes a familial trait

Sinus arrhythmias of respiratory origin, so easy to discover by comparing the pulse rates of inspiration and expiration, and the youthful arrhythmia of Mackenzie are commonly found in young people They are rarely discovered in individuals over thirty They are characteristic of normal hearts, commonly disappear as the heart rate is quickened by exercise or by belladonna, and are indicative of the knifelike balance in the vagal and sympathetic control of the sino-auricular node

PRECOCIOUS SYSTOLES AND PAROXYSMAL TACHYCARDIA

Whereas the sinus arrhythmias are characteristically found in the presence of a normal cardiovascular system, and are almost never found in individuals with diseased hearts, the precocious systoles and paroxysmal tachycardias are of little prognostic value, because they are found equally frequently in the presence of normal and diseased hearts They stand midway between what I might designate the normal or physiologic arrhythmias and the abnormal or pathologic irregularities that will be discussed in subsequent sections Paroxysmal tachycardia may be of auricular, nodal or ventricular origin, just as are the precocious systoles There is no difference in the mechanism of production, but in paroxysmal tachycardia the ectopic beats are for 'paroxysms" of varying periods of time without the intervention of normal complexes

It is probably true that if one could examine all patients with precocious systoles, it would be found that the majority of them would be relieved by giving up coffee and tobacco Students at the time of their fourth year examinations, when they are working long hours and often under the stimulation of coffee and tobacco, are worried frequently by this form of cardiac irregularity without subsequent evidence of heart disease A great many professional men become 'heart con

scious" in their early forties and fear angina The diagnosis of early angina is extremely difficult, but many times the patient's trouble is relieved by some simple hygienic measure, such as by the elimination of coffee and tobacco, by protection from mental strain, or by the regulation of exercise, food or habit of stool The therapeutic "lead" requires a most careful history of the patient's manner of life Nevertheless, whenever precocious systoles are found in a patient, it is the physician's responsibility to prove, so far as it is possible, that there is no organic heart disease, and probably it is wise to insist on a subsequent reexamination six months later, for precocious systoles can be the earliest symptom of actual heart disease A premonitory symptom of this kind, just as hemoptysis in lung disease, cannot be treated lightly If there is organic heart disease, there should be clinical signs such as cardiac enlargement, modification of the heart sounds, or evidence of decompensation within the six months' period, or there should be electrocardiographic evidence of heart disease, such as increased intraventricular conduction time or inverted waves in the first two leads

There have been investigations of the prognostic significance of the different types of precocious systoles The results have been inconclusive, but I feel that I would prefer to have the ventricular type, and would be less happy with the auricular precocious systoles, could I choose a particular kind of ectopic beat! Yet, interestingly enough, the patient with the ventricular type is frequently conscious of his "heart turning over" or of a "skipped beat," and rarely is a patient conscious of the nodal or auricular precocious systole Occasional patients with ventricular precocious systoles, where there is no evidence of heart disease and where all hygienic measures have been of no avail, are most unhappy and uncomfortable, for treatment is most unsatisfactory The application of an ice-bag to the precordium, and the use of mild sedatives are perhaps helpful, but constant reassurance and the pursuit of a reasonably interesting life, without too much responsibility, may prevent the patient's being conscious of the irregularity during the daytime,

and a mild hypnotic may impair the sensorium and reduce the discomfort that is most annoying, just before going to sleep

It is important to stress the significance of precocious systoles that may develop during the period of treatment of an underlying cardiac disease The possibility of digitalis poisoning is suggested by the appearance of precocious systoles, which are commonly of the ventricular type, and immediately there should be a review of the amount of digitalis that has been given

Auricular precocious systoles, in the presence of the signs of cardiac disease, sometimes are a premonitory warning of impending auricular fibrillation, and occasionally a patient will manifest this sequence of events It is, therefore, practical to test the value of quinidine in 5 to 10 grain doses, three times a day, in an attempt to clear up this type of irregularity The results are difficult to evaluate, for, even if successful in developing a normal rhythm, the physician should remember that the treatment of the underlying heart disease necessarily reduced the auricular stress that is an important etiologic factor in the production of auricular precocious systoles So that the therapeutic value of the quinidine is quite like the value of a drug employed by physicians who claim "to have averted pneumonia"

Although paroxysmal tachycardias resemble precocious systoles, the strain on the myocardium because of the persistence of the ectopic contractions and the mechanical interference with the blood supply to the organs of the body, especially to the brain, merit an increased effort to shorten the paroxysm Fortunately, most patients suffering with this arrhythmia have, themselves, learned procedures that commonly end the attacks Swallowing large globuses of bread or cereal, or drinking water in large gulps, probably by vagal pressure, may be efficacious Some patients at the onset of an attack can abort it by lying over a chair with their head on the floor, or by grasping the front of their neck between the thumb and forefinger Some have helped themselves by deep inspira

tions or by straining as if at stool. But when not successful in their efforts, or at the onset of the first attack, the aid of a physician is often sought Generally such patients are badly frightened, and just as calmness and reassurance are most salutary in the presence of gastric or pulmonary hemorrhages—for these symptoms are commonly self-limiting and death is quite unusual in the attack—so the physician should allay the fears of the patient and his family during an attack of paroxysmal tachycardia and undertake the different maneuvers that patients have found useful in terminating attacks Direct vagal pressure in the neck—pushing under the anterior belly of the sternocleidomastoid muscle at the level of the thyroid cartilage back of the carotid artery—will occasionally abort the attack, or pressure on the eyeball—again a vagal phenomenon—may be tried Probably such procedures are successful in only one out of fifty patients—much more rarely than textbooks would lead you to suppose If these attempts are unsuccessful, the patient should be put to bed and an ice-bag placed on his precordium Liquid diet should be given and the patient asked to swallow in large gulps It is wise to have the patient in a hospital or, at least, isolated from his family and protected from excitement Luminal or bromides are useful sedatives, and if the attacks persist for twelve hours, a hypodermic of ⅙ grain of morphine sulphate may put the patient to sleep The paroxysm may have disappeared before he wakens Digitalis is only indicated in the presence of organic heart disease, or when, after twenty-four or thirty-six hours, evidence suggesting early myocardial insufficiency should appear Certainly, the digitalis has no effect in stopping the paroxysm In general, then, paroxysmal tachycardia is self-limiting Protection of the heart by rest, reduced food intake, and the use of sedatives are the essential therapeutic procedures during an attack Later, every effort should be made to prevent subsequent paroxysms, and here, knowledge of the patient's manner of life, the treatment of focal infections, or the study of the gallbladder and gastro-intestinal action may provide the therapeutic "lead"

AURICULAR FIBRILLATION AND FLUTTER

These two arrhythmias can be discussed together They may occur during any acute infection or during thyreotoxic osis, subsequently to disappear and leave no evidence of cardiac disease Otherwise, they are definitely significant of, and always associated with actual disease of the heart muscle. In the latter case therapeutic measures as outlined by others in this symposium, are first indicated Whereas cardiac dis ease, in itself, is not an indication for the use of digitalis and its use may be harmful, cardiac disease plus fibrillation of the auricle, especially if the ventricular rate is faster than 80 per minute, always calls for the use of this drug The slowing of conduction rate in the His bundle resulting from the use of digi alis, protects the ventricle by aborting many of the auricular stimuli Thus the mechanical efficiency of the ventricle is improved, and the strain on the ventricular muscu lature from such rapid and ineffectual contractions is lessened When auricular fibrillation is present, the physician has a definite indication of the amount of digitalis needed After digitalizing the patient, there is no need to fear digitalis poisoning from too long-continued use of this drug for the ventricular rate, as ascertained by counting the contractions at the apex of the heart, should not be allowed to slow below 80 per minute To be sure, especially, in patients older than sixty years, auricular fibrillation may develop and the apex rate be very slow 60 or less per minute. Here we have an indication that heart block is already present—commonly, if the patient has not been overdosed with digitalis, significant of disease of the bundle of His from arteriosclerosis of the end artery that supplies this structure, or from infarction, or from coronary thrombosis In such cases, the presence of fibrilla tion is not an indication for the use of digitalis Its use would depend on the degree of myocardial insufficiency After the apex rate has been slowed to 80 or thereabouts, one can take up the question of the value of quinidine in an effort to bring about a normal rhythm While I am not prepared to state that digitalis itself can terminate auricular fibrillation and

bring about normal sinus rhythm, it is certainly true that, following therapy directed to the myocardial disease, which often includes the therapeutic use of digitalis, the normal sinus rhythm may supervene This, I think, is understandable For certainly we have abundant evidence to show that disease of the auricular musculature, or mechanical strain of the auricles—generally with stretching of their tissue and often sequential to mitral valve disease or emphysema—is followed by the development of the "circus movement" in the auricles—auricular fibrillation Relief of this strain by the reduction of the auricular load following cardiac therapy, may be the explanation of the resumption of normal sinus rhythm The point I want to make is that during the period of digitalis therapy it is not unusual for auricular fibrillation to be changed into a normal sinus rhythm without the use of quinidine I think this phenomenon is particularly apt to take place when the fibrillation has lasted less than a month before treatment and when the treatment of the myocardial disease or emphysema is efficacious On the other hand, where the myocardial disease is extreme and of long standing, auricular fibrillation, when present, may be converted into auricular flutter which is difficult to control, or the fibrillation may continue, no matter the therapy employed

The use of quinidine in the presence of a fibrillation that has persisted in spite of correct cardiac therapy, has certain contraindications In elderly patients—those above sixty—especially where one is dealing with arteriosclerotic heart disease, or hypertensive cardiovascular disease, quinidine is commonly unavailing If sinus rhythm is produced, it is notoriously short lived, and fibrillation reappears Moreover, there is the possibility, occasionally with disastrous results, that, when the auricle mechanically contracts—with the onset of sinus rhythm—emboli from thrombi in the left auricle may be whipped off, and carried by the arterial stream to different organs of the body Thus as a result of the temporary cure of the fibrillation, the patient may develop a cerebral accident or visceral infarction! Again, in younger patients where fibrilla-

tion has been present for longer than a year, the resumption of sinus rhythm as a result of quinidine therapy lasts a comparatively short time in most cases, even in spite of chronic quinidine therapy, and here also, unusual to be sure, there is the possibility of embolic phenomena Quinidine has been employed as a therapeutic agent for many years Although there is a definite field for its employment, for there is obvious improvement in the efficiency of the heart as the result of the supervention of the sinus rhythm, I wonder if its use is not too frequent It certainly seems as if the "breaking" of the "circus movement" is the result of a paralysis of the conduction mechanism of the auricular muscle—possibly a toxic mechanism—and, if this is true, one can well wonder as to the effect on other qualities of the heart muscle, especially when the muscle is already diseased I am suggesting caution in the use of quinidine and preparing you for the experience that it is often difficult to stop the fibrillation, and that resumption of sinus rhythm is often for short periods of time Auricular fibrillation or the perpetual arrhythmia as it used to be designated, is no longer regarded as significant of impending death I can remember when it was said that patients with this arrhythmia could not live for more than five years I have two patients, one now fifty and the other seventy two, who have had auricular fibrillation for twenty years and have lived reasonably active lives In both of them, quinidine was ineffectual in producing sinus rhythm

Personally, in using quinidine sulphate, I have always insisted first on the hospitalization of the patient and then, after instituting general cardiac therapeusis, have digitalized the patient's heart, slowing the rate to about 80 per minute Subsequently, I have discontinued the digitalis and given 4 grains of quinidine twice a day, for the first day, and then, if there were no evidence of quinidine idiosyncrasy, given 6 grains of the quinidine sulphate, four times a day

If during quinidine therapy the ventricular rate increases much above 80, it is necessary to stop quinidine and resume the use of digitalis If the fibrillation persists after a week of

quinidine therapy, it is well to discontinue this drug for a few days and use digitalis, if indicated by the ventricular rate Weekly courses of quinidine can be employed in this way But if sinus rhythm does not appear by the end of the third course, it is highly probable that the fibrillation cannot be broken If, however, sinus rhythm can be produced, quinidine should be gradually reduced Often such patients can be given chronic dosages of about 3 grains of quinidine three times a day The appearance of auricular precocious systoles or of an increasing heart rate, would indicate the discontinuing of quinidine and the resumption of digitalis

In recent years much larger doses of quinidine have been employed—15 or 20 grains four times a day—and the drug has been reduced in amount, immediately upon the resumption of normal rhythm Possibly a somewhat greater number of fibrillations can be broken by these large doses, but I am not convinced that the persistence of a sinus rhythm, where obtained, is of any longer period of time Just to get a sinus rhythm for a few hours or days is hardly worth the danger from emboli or from possible toxic effect of large doses of quinidine! It seems important to emphasize the individuality of each case of auricular fibrillation, and to advise you to make your therapeutic effort step by step, watching the reaction of the particular patient—*safe, individual therapeusis, rather than* the mechanical application of an arithmetical formula

Auricular flutter is a notoriously difficult rhythm to break Patients with this disorder often show transition from flutter to fibrillation, following the use of digitalis and occasional sinus rhythm will follow quinidine therapy But all too commonly flutter reappears Generally, the flutter continues in paroxysms or steadily, no matter what is done

Paroxysmal fibrillation or flutter appearing in patients during the fifth or sixth decades, and often associated with hypertensive cardiovascular disease, is a frequent discovery Treatment of the heart is indicated, chronic quinidine therapy is employed, but generally the result is that the patient soon shows signs of myocardial insufficiency and becomes a chronic

"cardiac," with permanent fibrillation The underlying disease is progressive and the symptomatic treatment gradually becomes unavailing

PARTIAL AND COMPLETE HEART BLOCK

Except for its transitory appearance during the course of some acute disease, heart block, either partial or complete, is significant of serious myocardial disease Intraventricular as well as auriculoventricular conduction blocking means widespread damage, involving the His bundle and its arborizing branches The diagnosis is rarely made clinically, except when there is complete block of the main bundle of His, electrocardiographic study is necessary for the diagnosis of partial block. Therapy directed toward the heart muscle is, in general, the important procedure and treatment of the arrhythmia itself is far less important. However, it must be remembered that the transition from partial to complete block or, in other words, the transition from sinus to ideoventricular rhythm constitutes a danger period—for the ventricle has "difficulty in learning" to institute its own pacemaking function Some of you will have the opportunity to save the life of a patient known to have heart block, whose heart has come to a standstill Epigastric massage of the right ventricle, or injection of adrenalin into the heart muscle, may supply the necessary stimulus to produce ideoventricular rhythm, when conduction of the sinus impulse along the His bundle has stopped In the presence of partial heart block, unless its use is imperative, digitalis is contraindicated This drug reduces the conductivity of the His bundle, and can be the final factor in producing complete block So even in first degree auriculoventricular block—only found by the aid of an electrocardiogram—it is wise to delay the use of digitalis, until myocardial insufficiency is definite

A common etiologic factor in the production of heart block, is gumma of the His bundle So until syphilis is ruled out potassium iodide in large doses is indicated The fact that the His bundle is supplied by an end artery favors the localiza

tion in that structure of gumma, in the presence of syphilis, abscess in the presence of acute infection, and infarction in the presence of arteriosclerosis When digitalis has been used and heart block has developed, one can try atropine or the tincture of belladonna to reduce the vagal activity with its consequent effect on the conductivity of the His bundle

PULSUS ALTERNANS

This arrhythmia when permanent, or when present for a few beats subsequent to an ectopic cardiac contraction is of ominous significance It is often found during the last two years of the life of a cardiac patient, particularly in those patients with progressive hypertensive cardiovascular disease or with arteriosclerotic heart disease There is no especial significance of this arrhythmia from the point of view of therapy, it denotes widespread myocardial damage, and is prophetic of the duration of life

CONCLUSIONS

It would seem, then, that you should remember that cardiac arrhythmias are not clinical entities, and that the group of sinus arrhythmias are characteristically found in the presence of normal cardiovascular mechanisms, that precocious systoles may or may not be significant of heart disease, that fibrillation, block and alternation are commonly to be found only in patients with heart muscle damage, and that there are contraindications, as well as indications, for the use of digitalis in the presence of a cardiac arrhythmia

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR HELEN B TAUSSIG

FROM THE HARRIET LANE HOME OF THE JOHNS HOPKINS HOSPITAL AND DEPARTMENT OF PEDIATRICS OF THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE

THE MANAGEMENT OF CHILDREN WITH RHEUMATIC HEART DISEASE (COMPENSATED AND DECOMPENSATED)

THE management of the child with rheumatic heart disease depends, not upon the valve involved, nor upon the severity of the lesion, but primarily upon whether or not the rheumatic process is active If the child is suffering from an active rheumatic infection, bed rest is absolutely essential If, on the other hand, the rheumatic process is entirely quiescent and the child is asymptomatic, he may, and indeed should, be allowed free activity Between these two groups of children whose management is diametrically opposite, there is an intermediate group composed of convalescent children who are in the transitional stage between complete bed rest and a normal active life. Let us consider separately each of these three groups

THE CHILD WITH AN ACTIVE RHEUMATIC INFECTION

Since the recognition of an active rheumatic infection is of prime importance in the management of the child with rheumatic heart disease, it is advisable to review briefly the signs and symptoms indicative of activity

The most common complaints are fatigue, malaise, joint pains, and shortness of breath In addition, some children complain of precordial pain and occasionally of palpitation, and in some instances, of abdominal pain or severe epistaxis

Malaise and *fatigue*, which are usually associated with fever, pallor, loss of weight, loss of appetite, and irritability, are symptoms common to all acute infections They do not

necessarily indicate active rheumatism However, if the child has rheumatic heart disease and there is no other obvious explanation for these complaints, they are, in all probability, due to an active rheumatic infection

Any *joint pains* in a child who is known to have had acute rheumatic fever, even though they are transient and not associated with redness or swelling, strongly point toward activity If these pains are associated with fever, it is almost certain that the child is suffering from active rheumatism Moreover, when the process is active in the joints, there is almost invariably an acute inflammatory process in the myocardium, although there may be no demonstrable evidence of this One is sometimes misled into believing that the heart has escaped without further damage because after a valvular lesion has developed, subsequent valvular injury and myocardial changes may be so insidious as to pass unnoticed until the onset of fibrillation or of myocardial failure

Shortness of breath, frequently manifested in the child by his inability to keep up with his playmates, is one of the early signs of myocardial failure On physical examination, the respiratory rate is almost always found to be accelerated, and if the respiratory rate is over 30 per minute, it is usually accompanied by some engorgement of the liver Moreover, a child virtually never develops cardiac failure from overexertion unless there is a concomitant acute inflammatory process in the myocardium Examination of the heart generally reveals some sign of an active myocarditis—such as tachycardia, gallop rhythm, some cardiac arrhythmia, poor quality of the heart sounds, a churning tumultuous murmur which extends from systole into diastole, a blurred third heart sound, or in occasional cases a high-pitched, screeching "sea-gull" murmur, or a pericardial friction rub, or an electrocardiogram may disclose some abnormality

All of these signs point toward an active rheumatic infection A child with rheumatic heart disease showing any of these signs should be put to bed and kept there until all signs of activity have subsided

Ideally, the child should have complete bed care. Practically, if the rheumatic flare-up has been mild—as for example, the child complained of mild joint pains which were readily controlled by small doses of salicylates and the heart action has remained quiet, complete bed rest is not absolutely essential. Such a child may be allowed to sit up in bed and play with toys and may even be carried to the bathroom. On the other hand, if there are clinical signs of an active myocarditis, complete bed care should be instituted. The child must be kept as quiet as possible. If he is not dyspneic, he should be kept flat on his back. He should receive the best possible nursing care, being fed, given a bed bath, and even being lifted on the bed pan. He should be allowed the minimum of toys and entertainment consistent with contentment.

Sedatives are indicated if the child is restless or overactive in bed. In the milder cases, luminal (phenobarbital) ½ to 1 grain three times daily may be sufficient. Sometimes the combination of luminal (½ grain) and aspirin (5 or 10 grains) will be found more effective than either given alone. Any form of sedative may be used provided the drug is both safe and effective, the purpose being to keep the child quiet. The more severe the myocarditis, the more imperative rest and quiet become. Many children with severe carditis are toxic and listless, they lie in bed almost motionless. Such children require no sedatives. If the child is not quiet, sedatives should be given freely. Under such circumstances, the most effective sedative is codeine. It may be given by mouth or by suppository—¼ to ½ grain twice daily, three times a day, or every four hours if necessary. It may be found advantageous to combine the codeine with luminal or trional. Sedatives should be pushed to the point that the child gets some sleep both during the morning and the afternoon as well as a long sleep at night.

The question whether *salicylates* are indicated in the treatment of rheumatic myocarditis is not settled. There is no evidence that salicylates alter the course of an acute carditis although, unquestionably, they reduce the inflammatory process in the joints. When there are joint manifestations, salicyl

ates are clearly indicated The dose should be gauged according to the severity of the joint pains Broadly speaking, 10 grains of salicylates per 10 pounds of body weight constitutes the maximum daily dose which a child requires Children under five years of age may require proportionally larger doses to control severe joint pains The total amount of salicylates should be given in divided doses during the first twenty-four hours The following day the dose of salicylates can usually be reduced by 20 per cent The form in which the salicylates are given is not important In my experience, aspirin is pleasanter to take and is better tolerated than sodium salicylate It is wise to combine sodium bicarbonate with salicylates when prescribing over 30 grains of salicylates per day For children under five years of age, it is advisable to combine any dose of salicylates with an equal quantity of sodium bicarbonate The rationale of combining sodium bicarbonate with salicylates has been challenged, but clinical experience uniformly indicates that salicylates are better tolerated when given in combination with some alkali

Whether sodium bicarbonate is given in tablets or in powdered form is of no great importance The powdered form (1 teaspoonful = 60 grains) has the advantage of being readily soluble in water and is easy for a child to take The administration of sodium bicarbonate has the added advantage that it acts as a mild laxative which is often desirable for bed patients

The above doses of salicylates all represent the average maximum doses Whenever joint pains can be relieved by smaller doses, there is no necessity to use large ones It has been my experience that the majority of children can be kept comfortable on 45 grains of aspirin a day, indeed, in many instances 30 grains daily suffices

After the administration of large doses of salicylates, our usual policy is to withdraw the drug gradually It is only the development of toxic symptoms which demands its abrupt withdrawal In every instance, whether the withdrawal is abrupt or gradual, a two-week interval must elapse after the medication has been stopped before one can tell whether the

rheumatic process has subsided or whether the pain has merely been relieved by salicylates It cannot be too strongly insisted upon that the child must be kept in bed during this period

In my clinic, other preparations such as the various cinchophen compounds have only been used in the rare cases of intolerance to salicylates

Pyramidon (amidopyrine) is sometimes useful in cases which require enormous doses of salicylates The practical advantage of the drug is its potency—six times that of salicylates The dose is proportionately small The greatest danger in the drug lies in the possibility of its toxic effect upon the white blood cells Recently a number of cases of agranulocytic angina have been reported in connection with the use of pyramidon or pyramidon in combination with a barbiturate Although this is not the usual effect of the drug, some people appear to have an idiosyncrasy to it. The number of people who respond in this manner is small, but the consequences are so serious that this possibility must always be borne in mind Because of the feeling that the barbiturates may aggravate the toxic effect of pyramidon, luminal or other barbiturates should never be prescribed with pyramidon Furthermore, it is essential to keep the patient under close observation A white blood count should be done before the administration of the drug, again three or four hours after the first dose, and daily thereafter A marked fall in the leukocyte count or a decrease in the percentage of the polymorphonuclear neutrophils demands the immediate withdrawal of the drug The clinical untoward symptoms are malaise, exhaustion, fever, or the development of a sore throat These complaints, also, demand the immediate withdrawal of the drug With these precautions, I believe it is safe to use pyramidon in children suffering from acute rheumatic fever in whom it is difficult to relieve the joint pains with salicylates The maximum total dose of pyramidon is 20 grains in twenty four hours given in divided doses This dose is usually decreased on the second day to 15 grains per day as a maintenance dose The maintenance dose should be kept as small as is compatible with the comfort of the child

The principal advantage of the drug is the ease of administration Obviously it is easier for a child to swallow 3 or 4 tablets daily than 20, especially when the 20 tablets require the addition of sodium bicarbonate

In giving pyramidon even to persons who show no idiosyncrasy to the drug, a daily divided dose of 20 grains of pyramidon should never be given for more than five weeks, although 15 grains daily can usually be given for six months without the development of toxic symptoms Upon the withdrawal of pyramidon, joint pains frequently recur within twenty-four hours, but in some cases there is a latent period of two weeks Therefore, the same rule should be enforced after the withdrawal of pyramidon as after the withdrawal of salicylates—namely, the patient must be kept in bed for the ensuing two weeks

MYOCARDIAL FAILURE

The development of congestive failure calls for specific therapy Under these circumstances, the question of the use of digitalis arises Digitalis is of little avail in the presence of a fulminating myocarditis When cardiac failure occurs in the course of an overwhelming infection, the improvement from digitalis is, at best, only temporary, and the heart failure recurs in a few days A number of cases of sudden unexplained death following the administration of the drug to such children have been reported Therefore, in cases showing severe toxic manifestations, digitalis is contraindicated

The real indication for the use of *digitalis* is in long standing chronic congestive heart failure which recurs on slight provocation In these cases the heart is enormously enlarged, and there is little or no cardiac reserve The slightest rheumatic flare-up or possibly even any increased work demanded of the heart will result in cardiac failure Digitalis under these conditions may be of great help and prolong life for many months, even for years

The other main indication for the use of digitalis is auricular fibrillation In cases of auricular fibrillation, the ventricular rate should be controlled by digitalis, the dose should be

adjusted to keep the rate between 70 and 80 per minute In children with rheumatic heart disease, the onset of auricular fibrillation indicates progressive myocardial damage. The presumptive evidence is, therefore, that the process is active, the child should be treated accordingly Once fibrillation has developed, it usually persists until the end There is no advantage in trying to revert the heart to a normal mechanism, for the underlying damage to the myocardium is so great that the heart will, in all probability, be unable to maintain a sinus rhythm For this reason, quinidine has no place in the treatment of children with rheumatic heart disease.

The usual adult dose of any digitalis preparation of standard potency (*i e*, 1 cc or 0 1 Gm = 1 cat unit) is 33 mg per kilogram but a child will frequently require as much as 45 mg per kilogram In estimating the probable requirement of digitalis, it is wise to calculate the dose both on the basis of the adult's and of the child's requirement The child will probably digitalize somewhere between these two amounts,[1] the exact amount depending upon the size of the child and the individual variation in susceptibility When administering digitalis for the first time, as a matter of precaution, the initial dose should be small in order to test the patient's sensitivity to the drug For rapid digitalization, this may be followed in two hours by a larger dose, the sum of these two doses equaling one third of the child s total requirement The remainder should be given in divided doses at intervals not closer than every six hours[2] Caution should be used as the total calcu

[1] For example A child weighing 40 kg would require 1.8 Gm of digitalis according to the child s requirement but only 1.32 Gm according to the adult standards A 40-Kg child is approaching adult size therefore he will probably require a total dose somewhere between 1.32 and 1.8 Gm

[2] For example A child weighing 50 pounds (22 7 kg) On the basis of 33 mg per kilogram total dose = 0 75 Gm on basis of 45 mg per kilogram total dose = 1 Gm Therefore give 0 1 Gm test dose After two hours give 0.2 Gm and six hours later give 0 2 Gm and six hours thereafter 0 1 Gm This means that at the end of twenty hours the child will have received the full effect from the 0 6 Gm given If not digitalized continue to give 0 1 Gm every six hours for three or four more doses provided there are no signs of toxicity Then place the child on a maintenance dose

lated dose is approached Usually there is no need for rapid digitalization, the total digitalizing dose may then be given slowly over a period of three days [1] When possible, it is helpful to check the progress of digitalization with electrocardiograms This is more important with a child than with an adult because the total required amount is less, and, therefore, the margin of safety is smaller

The therapeutic effect of digitalis is shown by general improvement When edema is present, the improvement is usually accompanied by a diuresis Sometimes there is an obvious decrease in the size of the liver and in the size of the heart. Usually there is an improvement in the quality of the heart sounds and often a disappearance of a gallop rhythm At this stage the patient should be placed on a maintenance dose of digitalis—this varies between 0 05 and 0 1 Gm per day with the complete omission of the drug for one or two days each week

Digitalis should not be pushed so far as to produce toxic symptoms If signs of toxicity develop—such as nausea, vomiting, dropped beats or other cardiac irregularities—digitalis must be withdrawn Thereafter, no digitalis at all should be given until all signs of toxicity have disappeared Then, and then only, should the patient be placed on a maintenance dose

The various other manifestations of myocardial failure each call for specific treatment *Cough* usually occurs early and is liable to be troublesome It disturbs the patient's rest, and the effort of coughing throws an additional burden on the already failing heart First of all, placing the child in the erect position usually gives some relief Codeine is the drug of choice Often it is more effective when given in combination with terpin hydrate When administered in this form, the

[1] For example For slow digitalization of the same child (50 pounds), give 0 1 Gm three times daily at six-hour intervals (8 A M, 2 P M, and 8 P M, or 10 A M, 4 P M, and 10 P M) for three days On the fourth day give 0 1 Gm in the A M and, if necessary, this may be repeated at night Thereafter the child should be placed on a maintenance dose In this case the maintenance dose would probably be 0 05 Gm per day, six days a week

codeine content of the compound may be increased above the standard solution of 1 grain per ounce of terpin hydrate Digitalis, through improvement of the pulmonary circulation and by decreasing the size of the heart, is often of great help Not infrequently infection as well as congestion is present, under such circumstances a steam tent may give relief

In cases of failure with congestion, an effort should be made to decrease the *edema* When the patient has failed to seek help until after the development of edema, simple bed rest and the limitation of fluids to 500 or even 300 cc per day may result in great improvement. If these measures are not effective, the administration of digitalis should be considered As previously stated, if the heart failure is due to an overwhelming infection, digitalis is of doubtful value If, on the other hand, the failure is the result of a long-standing infection and the gradual diminishing of the cardiac reserve, digitalis may improve the circulation producing the desired diuresis and the concomitant loss of edema

If these measures are of no avail, *diuretics* should be tried The perfect diuretic has not yet been found Theobromine (0 3 Gm three times daily) or theocalcin (0 5 Gm three or four times daily) may be tried All such drugs require several days to produce diuresis When prompt action is desired, *salyrgan* is the most effective drug Salyrgan (0 5 cc to 1 cc.) should be given *intravenously* diluted 1 10 in normal saline This lessens the danger of thrombosing the vein Furthermore, if there is any extravasation, an additional 10 cc. of normal saline injected subcutaneously about the site of the vena puncture will prevent the development of a slough Salyrgan acts promptly, producing its maximum effect within twelve hours, it should be given in the morning in order not to disturb the patient's rest at night. The effect of the drug is usually of short duration and may require repeated administration The effectiveness of salyrgan may be increased by the previous administration of ammonium chloride (5 grains three or four times a day for a period of three or four days prior to the administration of salyrgan) When giving salyrgan repeatedly,

the urine must be closely watched for evidences of renal damage In cases of severe renal damage, salyrgan is contraindicated Under such circumstances, hypertonic glucose (10 to 20 cc of a 50 per cent solution) may be given intravenously Its action, however, is not as constant as that of salyrgan

In cases where the edema is massive and fails to yield to these measures, Southey tubes may be inserted into the dorsum of the feet or into the legs Provided novocain (1 per cent) is used to anesthetize the area, the procedure is entirely painless The tubes are left in place for twelve to twenty-four hours Even though but little drainage is obtained during this time, the puncture wounds produced by the tubes frequently drain for days after and thus effectively reduce the edema The danger in this procedure is infection Therefore, this treatment must be carried out with rigid asepsis, and the wounds should be dressed with sterile dressings until entirely healed Because of the danger of infection, this treatment is contraindicated in cases of thrombosis or of an obstructed circulation

Venesection is imperative in cases of pulmonary edema and may give relief in cases where venous engorgement of the neck vessels remains pronounced when the patient is sitting bolt upright Under these circumstances, 3 to 4 cc of blood per kilogram of body weight (*i e*, 1 5 to 2 cc per pound) may be withdrawn by the same procedure which is used for obtaining blood for a transfusion Although the venous pressure rises rapidly again, the clinical relief from this procedure usually lasts twenty-four to forty-eight hours

When cyanosis becomes pronounced, *oxygen* may make the patient more comfortable Theoretically, oxygen should be of great benefit to a patient with a low vital capacity Practically, the results are not as brilliant as might be anticipated Oxygen is of no value if it is given by a funnel, and it is virtually of no value when given by a nasal catheter It should be given by means of a tent, and even when so given it seldom alters the course of the disease The explanation of this may be that it has been employed only as a measure of last resort when too late to influence the course of the disease

All of the procedures in the preceding paragraphs are recommended in order to make the patient more comfortable and are used in the hope of tiding him over until the subsidence of the acute infection If the child is desperately ill and the outlook is hopeless, the child should be made as comfortable and as happy as possible All procedures which disturb the child should be abandoned Sleep is the greatest blessing Morphine (by hypodermic, 1 mg per 5 Kg of body weight) or paraldehyde (4 to 8 cc. by rectum) may be found advantageous to produce the desired sleep Under no circumstances should the child be permitted to sense that the situation is hopeless Occasionally even in the most hopeless cases, an extraordinary unexpected change for the better will occur If and when the acute inflammatory process does subside, there will be clinical improvement The edema and cough will disappear, and the child will slowly begin to mend

THE CONVALESCENT CHILD

The most perplexing problem in the management of children with rheumatic heart disease is how long to keep them in bed The principal difficulty lies in determining how long the infection is active. The minimum requirement before a child is allowed to be up at all is two weeks off medication and free from all symptoms and signs of an active rheumatic infection This means not only that there has been no recurrence of joint pains or any other rheumatic manifestations, but also that the heart has shown no evidence of an active infection, that the temperature, pulse, and respirations have remained normal throughout the period, and that all laboratory tests prove to be normal

The obvious rheumatic manifestations—such as joint pains, severe epistaxis, rash, and nodules—are easy to determine. The difficulty lies in the recognition of the presence or absence of a myocarditis and in the determination of the temperature, pulse, and respirations which indicate an active infection

No infallible method exists for ascertaining the presence or

absence of a *myocarditis* There are, however, several helpful findings The murmurs of valvular lesions are clear cut and definite when the heart is well compensated Sometimes it is difficult to determine whether a sound in diastole is a pathological third heart sound, an incipient mid-diastolic murmur, or due to the presence of a gallop rhythm The origin of such a sound is of academic interest, all of them indicate active rheumatism After the infection has subsided, a gallop rhythm disappears There is no confusion of sounds and murmurs, it is easy to separate the systolic from the diastolic murmur A third heart sound may persist but that is a definite sound, not such as to be confused with a murmur From week to week and month to month, the murmurs remain the same Changing murmurs or the development of new murmurs indicate persistent activity, or such a recent process that the child should be treated as if the infection were still active

The *electrocardiogram* frequently offers additional evidence of activity It is of well defined but not conclusive aid While an abnormal electrocardiogram indicates definite pathological changes, a normal electrocardiogram does not necessarily mean that the heart is normal The commonest abnormality which the electrocardiogram reveals is a delayed conduction between auricle and ventricle Inasmuch as there is no clinical method of determining this condition, the heart cannot be conclusively pronounced normal unless the clinical findings have been confirmed by an electrocardiogram A conduction time of 0 2 second is the upper limit of normal for an adult, 0 18 second should be considered the upper limit of normal for a child of ten years or under Not infrequently in children with rheumatic fever, a prolonged conduction time is so persistent that it is liable to be interpreted as a permanent phenomenon due to scarring rather than as a manifestation of an active infection Such a deduction is not justifiable until after a test period of several months of bed rest has been instituted During this time other factors indicative of the presence or absence of activity should be watched for—as for example the evidence to be derived from the temperature, the pulse, and the respiratory rate

What constitutes normal temperature, pulse, and respira tions? The easiest of these three questions is that concerning respirations The trouble in evaluating respirations is not in determining what is normal, it is failure to count them The normal *respiratory rate* for a child as well as an adult is 20 to 22 per minute Twenty-four per minute may be taken as the upper limit of normal Many children with heart disease will breathe very rapidly—at 30 or even 40 per minute—yet so quietly that unless regularly and carefully sought for, this rapid respiratory rate passes unobserved

What constitutes the normal *temperature* and the normal pulse rate is much debated When the question is raised in regard to children with acute rheumatic fever, the problem is especially perplexing because, except for the cases with very severe infections, a low grade fever (about 100° F) is the rule Hence, the child should not be allowed to get up at all until the daily temperature for a two-week interval has not reached 100° F by mouth or exceeded 100° F by rectum Further- more, a child who is convalescing from acute rheumatic fever tends to develop a fever from causes which would not affect a healthy child—such as slight fatigue or undue excitement This abnormal febrile reaction probably means that the process is not entirely quiescent Throughout convalescence the tem perature should, therefore, be used as a guide in regulating his activity When the entire illness is over and forgotten, the temperature as well as the pulse rate does return to normal (98 6° F) In addition to the height of the temperature, the extent of the daily fluctuation is sometimes emphasized as sig nificant This phenomenon is most pronounced during the period of obvious Infection The swing diminishes as the infec tion subsides

The normal *pulse rate* for a child lies between 80 and 90 per minute The child should be kept in bed until the pulse rate is below 100 per minute Difficulty arises in the cases in which the heart rate continues above 100 per minute for a long period of time If, however, the temperature as well as the pulse rate remains a trifle elevated, probably both are due

to a persistent low grade active infection rather than to any extraneous cause A persistent tachycardia is not infrequently regarded as of psychic origin In considering this possibility, the sleeping pulse rate yields valuable information During sleep a psychic tachycardia entirely disappears, whereas, one of rheumatic origin will drop but 4 to 8 points Another helpful test is the response of the heart to some simple exercise—as for example, hopping on one foot for one-half minute The normal heart accelerates approximately 10 to 25 beats per minute and returns to the resting rate within two minutes A poorly functioning heart will usually accelerate markedly in response to such exercise and will not return to the resting rate for five, ten, or even twenty minutes

The *white blood count* sometimes serves as another indication of activity It is one of the least reliable criteria because of the normal fluctuations of the leukocytes and, also, because an active infection may persist without a leukocytosis For this reason, while a leukocytosis is of positive value in indicating an active infection, a normal white count does not necessarily exclude it

Recently the *sedimentation rate* of the red blood cells has been advocated as a significant test in determining the presence or absence of activity At the present time, one cannot speak with finality upon this subject There is, however, a growing feeling that the test measures one of the most persistent of the abnormal features of the disease It must be remembered that an accelerated sedimentation rate is not pathognomonic of a rheumatic infection but may occur in any illness Its value lies in establishing the significance of fleeting joint pains or in indicating whether a known infection is still active

The rheumatic process should not be considered inactive until all of these abnormal conditions have disappeared Long before the process has entirely subsided, the child feels well A slight temperature, tachycardia, or even polypnea may persist for months without causing the child to feel ill Throughout this period the child becomes more and more active in bed The main problem resolves itself into that of preventing the child from getting up too soon

The first *increase in activity* is to allow the child to lie on a couch or to sit in a chair daily for one half hour Not infrequently the child is quieter on a couch than in bed If so, this treatment may be instituted before the temperature and the pulse rate have returned to normal On the other hand, if the slight additional strain which sitting in a chair entails causes a rise in the temperature or pulse rate, it must be abandoned until these are normal Once the child responds well to this increase in activity, the period of time during which he sits up may be gradually increased until he sits up in a chair for two hours a day It makes no great difference whether the child is allowed to be up in the morning or the afternoon My policy is to allow the child up in the afternoon since he can then look forward to the change throughout the morning After the child is up in a chair for two hours a day, no further increase should be attempted for the next two weeks Only provided the temperature, pulse, and respirations remain normal and the child remains asymptomatic during this two-week interval is a further increase to be recommended

The next step is to allow the child to walk across the room or to the bathroom (provided the bathroom is on the same floor and reasonably close to the child's room) He should begin by walking to the bathroom once a day and increase this very slowly, not more rapidly than one trip every other day, until he is walking to the toilet as often as necessary (six or seven times a day) When this stage has been reached, no further increase in activity should be prescribed for another two weeks

Thereafter, provided there is no recurrence of any rheumatic manifestations, the child may be allowed up two hours in the morning as well as two hours in the afternoon This increase in activity should again be followed by a two-week interval The child may then be allowed to remain up for the noon meal, or to be up three hours in the morning and then three hours in the afternoon or he may be allowed to do a little more while he is up

The question is frequently asked how soon the child may

be allowed to go out-of-doors The answer depends entirely upon the available facilities If the bed can be wheeled out on a porch, the child may be taken out whenever the weather permits On mild sunny days, fresh air and sunshine are undoubtedly healthful Sun baths, when possible, are beneficial The sun baths at the beginning should be brief and the time of exposure to the sun should be gradually increased The time out-of-doors, however, may be much longer, indeed, as long as the child desires, provided there is no sign of undue fatigue, or any untoward symptom On the other hand, if being out-of-doors means that the child is dressed and playing in the yard, the time outside should be strictly limited at the beginning to one-half hour The further increase in the allowance of out-of-doors activity should be regulated by the response to this exertion

The following tentative schedule is intended as a guide for a child who is convalescing from an acute rheumatic myocarditis This schedule is to be followed only provided the child remains asymptomatic throughout the entire period

1st month	1st two weeks	Up in a chair two hours in P M
	2nd two weeks	Up in a chair two hours in P M Walking to bathroom
2nd month	1st two weeks	Up in a chair two hours in A M and P M. Walking to bathroom
	2nd two weeks	Up 10 A M to 1 P M and 3 to 5 P M. This generally includes being up at the table for the noon meal
3rd month	1st two weeks	Up 10 A M to 1 P M and 3 to 6 P M
	2nd two weeks	Up 10 A M Out-of-doors 11 A M to 12 noon Lunch 12.30 P M Bed 1 to 3 P M Up 3 to 6 P M
4th month	1st two weeks	Up 10 A M Out-of-doors one to two hours A M and P M Two hours rest in P M Bed 6 P M
	2nd two weeks	Up 9 A M Two hours P M rest. Bed 6 P M
5th month	1st two weeks	Up 7 45 A M Two hours P M rest Bed 6 P M
	2nd two weeks	Up 7 45 A M School in A M (½ day) Two hours P M rest Bed 7 P M.

This schedule indicates that convalescence from acute rheumatic fever is a long slow procedure. The above precautions are necessary because of the difficulty of knowing when the process finally becomes inactive and because of the great danger of exacerbations The temptation always is to increase the child's activity before the process is entirely quiescent. In order to obtain the necessary cooperation from the parents, the danger of progressive rheumatic heart disease should be explained and, at the same time, emphasis should be placed upon the importance of getting the child well

If the infection has been mild and the child's activities are more rapidly increased, he must be kept under careful scrutiny for signs of a rheumatic myocarditis

When the child is treated conservatively, he is not ready to return to school for at least five or six months after a rheumatic infection Frequently a much longer period is required before the return to *school* The precise time when a child may return depends not only on the severity of the infection but also on the distance to school and the amount of stair climbing The child should always have undertaken as much exercise at home as his attendance at school entails before he is permitted to return to school It is, also, most important to bear in mind that upper respiratory infections are rife in all schools in the winter months Such *infections* are a real menace to the rheumatic child, all too frequently precipitating an exacerbation or recrudescence of the rheumatic infection It is, therefore, in general a wise policy to arrange for home instruction and to postpone the return to school until the spring The average child at public school can readily make up the studies he has missed during February and March and can pass the work given during the half year provided he returns to school in April This is usually possible even if for the remainder of the year he attends school only for one half of each day

As regards infection, what applies to the schools applies even more strongly to all large public gatherings—such as "movies" and theaters These entertainments are not essential for the child's education, and they are a potent source of

respiratory infections The parents should be warned of this danger

Should the child develop any intercurrent infection, he should be put to bed for a couple of weeks In addition, he must be kept under close observation not only during that illness but, also, for the *ensuing month* Ten to twenty-one days after such an illness is the time when the signs of reactivation of the rheumatic process most frequently become manifest The importance of keeping the child under observation during this period cannot be too strongly emphasized

The frequent exacerbations and recurrences of the rheumatic infection are what make convalescence so troublesome If a child's activities are increased too rapidly, the strain is liable to cause a return of fever, tachycardia, or some untoward symptom which will necessitate going back to bed and beginning over again As mentioned above, upper respiratory infections or any intercurrent illness is liable to precipitate an exacerbation of the rheumatic process Indeed, sometimes a flare-up of the rheumatic infection occurs for no apparent cause Regardless of the cause, the treatment is the same, the only thing to do is put the child to bed

The prevention of the exacerbations and recurrences of infection is the most important factor in the life of the child with rheumatic heart disease If this could be accomplished, the major danger of acute rheumatic fever would vanish Inasmuch as neither the etiology nor the mode of transmission is known, the most that is possible today is to establish and maintain a high level of general health and to keep the child free from infections The majority of the children who have been sent to Florida did well while they were there, but many of them have suffered from a recurrence of infection shortly after returning to the north

It is, therefore, important to institute a well-regulated day with healthy habits of eating, sleeping, playing, and studying At the same time, an effort should be made to direct the child's training along such lines as will enable him in later years to have a suitable occupation—not one involving heavy manual

labor, exposure to damp and cold, or constant exposure to upper respiratory infections

Foci of infection should be eradicated The teeth should be properly cared for and tonsillectomy considered Whether tonsillectomy is of value in the prevention of reinfection is open to question Diseased tonsils should be removed In border line cases, the decisive factor is the frequency with which the child suffers from upper respiratory infection In no case should tonsillectomy be attempted until convalescence is well established

THE CHILD WITH AN INACTIVE RHEUMATIC INFECTION

The management of the child with completely quiescent rheumatic heart disease is a simple matter If the child shows no symptoms or signs of an active rheumatic infection and has a good exercise tolerance, he may, and indeed should, be permitted free activity He must learn to live within his strength and be cautioned against undue fatigue. The only restriction that I place upon such a child is that he should never undertake what a normal child would find exhausting

The danger in handling these children lies not in permitting free activity to the well child but in the failure to recognize a smouldering active infection Regardless of how well a child appears to be, the process should not be assumed to be inactive until the child has been examined with care and all known tests for determining the presence of activity have been found to be normal As a final precaution, the child should be reexamined in a month's time to make certain there is no change

Finally, there remains to be considered the child whose heart is so severely damaged that he never becomes entirely asymptomatic. Children of this type have enormous hearts with little or no cardiac reserve, the majority of them always suffer from dyspnea on exertion Many of these children have an adhesive mediastinitis Whether cardiolysis is ever indicated in cases of adhesive mediastinitis of rheumatic origin is uncertain Usually the damage to the myocardium is so extensive and the liability of exacerbation is so great that cardiol

ysis is of little or no value Certainly such a procedure should not be undertaken in the presence of an active infection It is, indeed, difficult to determine whether heart failure in these children is due to a low grade active infection or to mechanical failure By and large, these children with enormous hearts, with or without an adhesive mediastinitis, compose the group who are benefited by digitalis If so benefited, it is wiser not to risk upsetting their equilibrium than to attempt to withdraw digitalis If digitalis is withdrawn, the child must be kept under close observation for six weeks It takes three weeks for digitalis to be entirely excreted The ensuing three weeks are critical as regards gradual mechanical failure In general, I prefer to allow these children with enormous hearts and little or no cardiac reserve up and about maintaining compensation with the aid of digitalis to keeping them in bed and compensated without digitalis During an acute exacerbation and for many months thereafter, they must be given complete bed rest As soon as their condition permits, it is justifiable to increase their activity in accordance with their exercise tolerance Their dyspnea limits their activity, there is no necessity for the doctor to do so Inasmuch as their prognosis is hopeless, it is the part of kindliness to grant them the maximum possible enjoyment of life

In contrast to these children, the children with a mild rheumatic infection and those with little or no cardiac enlargement have a good prognosis If only the active rheumatic infection completely subsides, this latter group of children, including those with valvular damage but without great enlargement, will not be seriously incapacitated They can look forward to a normal life Every possible effort should be made to get them well

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR EDWARD P CARTER

JOHNS HOPKINS HOSPITAL

THE USE OF DIGITALIS IN VARIOUS CONDITIONS

IT IS probably correct to say that few—if any—remedies have received the minute and detailed study over a period of 150 years that has been devoted to digitalis Certainly no single cardiac remedy has been so critically discussed or has been submitted in the same way to both clinical and experimental proof Knowing no more than these bare facts one would, I think, be quite justified in assuming that under the circumstances there must be at least very general agreement as to the indications for its clinical application, and no, or but few, differences of opinion as to the method of choice in its exposition and in the interpretation of the effects obtained following its administration And yet it is undoubtedly true that in spite of all the experience of years of clinical use and the intensive clinical and experimental studies there still remains a wide divergence of opinion as to its usefulness in certain clinical conditions together with, on the other hand, an extraordinary universal agreement as to its worth as the most important and valuable of any of the drugs having a direct influence upon the circulation It is also true that the differences of opinion referred to may be based upon a perfectly justifiable difference of interpretation

It is of further interest that with the single exception of *bufogin*, obtained from the tropical toad, the glucosides which so strikingly exercise their physiologic effect upon the myocardium are of vegetable origin We are told that the origin of the name "foxglove," the pseudonym for *Digitalis purpurea*, was probably derived from the term "folk's glove" or "faries'

glove," and that the German name "Fingerhut" (thimble) suggested to Fuchius, who first gave it its botanical description in 1542, the Latin adjective "digitalis" It is interesting that in Ireland it is called "Fairy thimble" and in Wales "Elves' glove"

The modern exposition of the drug is based upon a biological assay carried out upon the frog or the cat, more rarely the pigeon, which determines the strength of a given specimen as the calculated lethal dose of the drug in milligrams per frog or per kilogram of cat in terms of the so-called "frog" or "cat unit" The calculated average dose for clinical use is estimated at 0 15 of the cat unit per pound, or 0 33 per kilogram, of body weight It is further assumed that the theoretical strength of the cat unit should approximate the standard of 100 mg of the drug Accepting this measure as correct the calculated dosage for the average individual of 70 Kg or 154 pounds weight is easily determined as 23 1 cc of the tincture or 2 3 Gm of the powdered leaf [9, 10]

The early observations upon the drug date from the publication of Withering's monograph in 1785, a marvellously keen and discriminating clinical study which stimulated much interest and discussion at the time and can be read today with great profit It is indeed remarkable that many of Withering's conclusions are as applicable after all the lapse of years as when first stated The modern recognition of the problems involved in the therapeutic use of the drug may be said to date, in a way at least, from the time when the nature of auricular fibrillation was first clearly described by Cushny[8] (1906 and 1907) and following Mackenzie's[16] early contributions (1905 to 1911) Our clinical knowledge was further greatly facilitated by the development of Einthoven's string galvanometer which has made possible countless studies having to do with every phase of the specific action of the drug upon the myocardium

Physiological Action—No attempt to formulate any rules for guidance in the use of digitalis can be discussed without a brief statement as to its physiological action upon the heart We must remember that digitalis acts upon the myocardium in

two ways, (*a*) directly and (*b*) indirectly, and that of these two quite distinct effects, the latter *indirect,* resulting from its action upon the vagus, plays a most important rôle in the control of conduction and of the cardiac rate, the rate of ventricular response being influenced by stimulation of the vagus fibers in the junctional tissue and under some conditions the rate of the whole heart being modified by stimulation of the vagus center in the medulla Upon the junctional tissues, then, digitalis acts indirectly through the vagus giving rise to a lengthening of the conduction interval, while upon the auricular muscle the effects are such as to modify, by vagal stimulation, the rate of the intra auricular transmission, to shorten the refractory period of the auricular muscle and to increase the rate of auricular oscillations, this is the predominant effect and is illustrated by the diagram below It is chiefly to the agency of the vagal stimulation that the brilliant results in the presence of auricular fibrillation are due [12]

Effect of Digitalis upon the Auricular Muscle

	Rate of transmission	Refractory period	Expected rate of auricular oscillation	Usual result
Indirect	−	−	+	+
Direct	+	+	−	occasionally — or 0

In addition, however, to these striking evidences of its indirect effect, concerning which there is a certain unanimity of opinion, we recognize also a direct effect referred to above, which plays an equally important role but concerning the intrinsic mechanism of which, both chemical and physical, there is perhaps less unanimous agreement

The ventricular slowing following digitalis in the presence of auricular fibrillation was early recognized as primarily due to impairment of conduction from vagal stimulation. When, however, it was discovered that in these cases the ventricular escape following atropine was less after digitalization than before, the opinion was advanced by Cushny[7] and his school that this result was due, in part at least, to a direct effect upon

the myocardium, an opinion that was stoutly challenged by Lewis[12] and his group, who argued that in these instances in which the ventricular rate after atropine was less than before the exhibition of the digitalis, sufficient atropine to paralyze the vagal endings had not been given Be this as it may, the fact remains that it is in the presence of auricular fibrillation that one encounters the most striking results from digitalis therapy There are many instances when in the presence of a normal sinus rhythm the use of the drug is amply justified, but when its administration is not accompanied by any conspicuous clinical sign and certainly without any significant change in cardiac rate It is recognized today that the effect of digitalis upon the circulation is represented by the interplay of very diverse actions, the result, in any given instance, of a large number of variable forces Considering the dynamics of the circulation, apart from the effect of vagal stimulation, we know that the heart may be smaller, the output per beat may be reduced or even increased, as may the output per minute depending upon the initial size of the heart, the state of the myocardium and the degree of cardiac slowing [5 6]

The active glucosides obtained from the leaves may be given as a *tincture* or as the powdered leaf—the latter form being our method of choice—or as one of the many preparations available In any case accurate knowledge of the strength of the preparation employed is of the utmost importance Unfortunately, in the past there has been a wide discrepancy between the advertised and the true potency of a number of standard preparations of the drug [14]

We use a modified form of the body weight method of Eggleston and believe in giving moderately large doses in order to secure effective results fairly promptly That one may, rarely, encounter susceptible individuals is of course true, but there is usually some sort of warning and we never have seen harm follow from an overlarge dose Even after the extensive use of strophanthin or ouabain we have seen no untoward results, though it should be emphasized that, when using the latter preparations, one should be certain as to any previous digitalis

therapy, there being always the potential possibility of releasing the cumulative effect of the drug

Indications for Use—In so far as the acute demand is concerned the indications for digitalis are today universally recognized as depending upon the degree of cardiac failure rather than upon the type, though it is common knowledge that the most dramatic results are seen in the congestive failure associated with auricular fibrillation The drug may be given as an initial dose in the form of the tincture in 4 to 8 cc. doses or in the form of the powdered leaf in 0 4 to 0 8 Gm doses, to be followed in four to six hours by 2 cc or 0 2 Gm , the preparation of choice being continued in similar amounts four times a day until the desired effects are obtained or until the total calculated dose has been given

When giving digitalis one watches for the signs of its clinical absorption and particularly for any evidence of toxicity or of unusual susceptibility on the part of the individual to the drug The borderline between a conspicuous therapeutic effect and the minor symptoms of toxicity is often very slight The common symptoms of overdigitalization comprise the nausea and gastro intestinal distress often with vomiting, the occurrence of certain irregularities as premature beats and particularly the so-called "bigeminal rhythm" due to coupled beats, and as shown by means of graphic records early, delayed conduction or evidences of heart block The slowing of the heart rate to 60 or below is also a sign of digitalis effect The alteration in, and actual reversal of, the T wave in the electrocardiographic record is a further measure of the digitalis absorption by the myocardium It is of interest that in the experimental animal it has been shown that inversion of the T wave appears when 25 per cent of the minimal lethal dose has been given, prolongation of conduction after 50 per cent, premature beats after 70 per cent and complete heart block after 80 per cent [3] With the appearance of any evidence of overdigitalization the drug is of course withheld

When, in the presence of extreme congestive failure, with marked splanchnic engorgement, there is evidence of an ex

cessive irritability of the myocardium as shown by many premature beats and occasional coupling, one may proceed to complete digitalization, when, however, there is a history of previous recent digitalis therapy we do so cautiously In the presence of auricular fibrillation the effect of digitalization as evidenced by the ventricular slowing, by the increase in the urinary output, by the decrease in edema and of moisture at the lung bases posteriorly and by the relief of cyanosis and disappearance of the pulse deficit are often conspicuous

Under certain conditions, in failure with a normal sinus rhythm, when digitalis has been given in fairly large amounts, the direct effect of the drug may exceed the indirect in its action upon the auricular musculature, giving rise to areas of localized block and we may then encounter the onset of auricular fibrillation This seeming paradox is made use of in the treatment of auricular flutter in which condition we give digitalis to the therapeutic limit with the purpose of converting the flutter into an auricular fibrillation The drug is then withdrawn and in a certain percentage of instances, after a variable interval, the fibrillation ceases, giving way to the restoration of a normal sinus rhythm In this connection reference may be made to the possible causal relationship of digitalis therapy to the occurrence of auricular fibrillation in a certain number of established cases [18]

In the presence of congestive failure and a normal sinus rhythm the indications for the exhibition of the drug are usually quite clear, but the evidence of the therapeutic result is often much less conspicuous, though rarely it is surprisingly plain The argument has been advanced, in the past, that digitalis sometimes led to a rise in the peripheral blood pressure and hence, and because of the assumed slowing and resulting lengthening of diastole, should be used with great caution in the presence of aortic insufficiency Today fortunately this teaching is exploded, and we know that the quite common effect in a great many cases with normal sinus rhythm is to bring about a fall in the blood pressure together with the general improvement (Fig 170) Although an increased diuresis so often

follows digitalis administration it cannot be attributed to any more specific result than the general improvement of the circulation due to the primary cardiac effect.

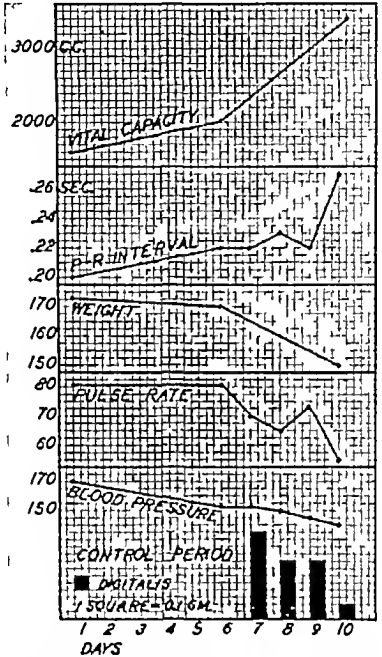


Fig 170.—G H., colored male age forty five Diagnosis Syphilis syphilitic aortitis, aortic insufficiency and myocardial failure Therapeutic result Disappearance of dyspnea and of rales from lung bases posteriorly diuresis with loss of edema and decrease in body weight, slowing of cardiac rate and improvement in vital capacity Weight Oct 31 63 4 Kg Digitalis 0.047 Gm per kilogram of body weight

With this very brief resume of digitalis action may we refer more specifically to various clinical conditions in which there is perhaps less agreement as to the indications for its

use We would emphasize again the statement outlined above that cardiac failure characterized by breathlessness on exertion, with cyanosis, with râles at the lung bases, with venous engorgement, with hepatic congestion and edema is sufficient evidence of the need for digitalis, although in the absence of auricular fibrillation one must not expect the same objective evidence of change in the heart rate The therapeutic effect is evidenced by diuresis with the loss of edema and decrease in the body weight, the disappearance of dyspnea and orthopnea and of congestion at the lung bases and decrease in the size and tenderness of the liver together with improvement in the vital capacity

Occasionally the question arises as to the use of digitalis in cases of heart block, either simple delayed conduction or complete A-V dissociation, when accompanied by the evidences of circulatory embarrassment The writer has always insisted that, when given with due regard to the condition, its use was perfectly proper Occasionally we have seen the conduction improved with the recovery of the cardiac failure With complete heart block there is not the same necessity for overcaution, since with complete A-V dissociation already established the vagal effects on conduction cannot increase the degree of block

We have already referred to auricular flutter and alluded to the traditional method of digitalis therapy, one of the exceptional conditions in which the drug may be used for a specific purpose in the absence often of any clinical evidence of circulatory failure The drug is pushed to the limit in the hope of converting the mathematically regular circus movement to the totally irregular rhythm of auricular fibrillation—4 to 6 cc. (0 4 to 0 6 Gm) being given daily to the point of complete digitalization In some cases it has required a total of from 72 to 96 cc of the tincture, over a period of two or three weeks, before converting the flutter into fibrillation [22] These amounts are, of course, exceptional, but since the total dosage is spread out over a fairly long period of time are often surprisingly well tolerated Occasionally the onset of nausea or

other signs of toxicity may necessitate withdrawal of the drug before fibrillation is induced It quite often happens, however, that fibrillation occurs after the drug has been stopped

The typically characteristic course of a case of circulatory failure with normal sinus rhythm, due in this instance to cardiovascular hypertensive disease, is illustrated in Fig 171 Here it is seen that while the weight decreases, and the vital capacity

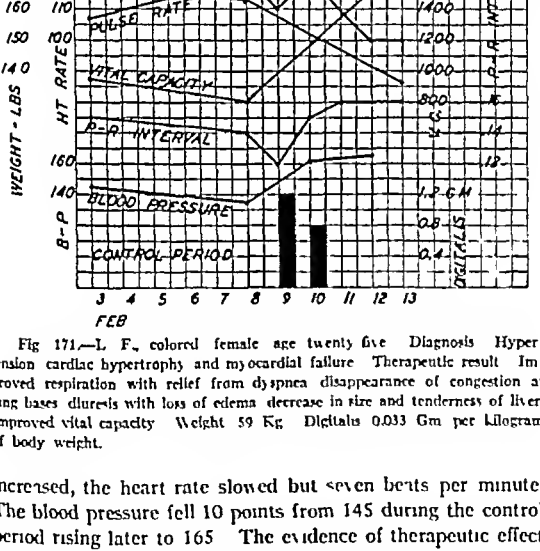


Fig 171.—L F., colored female age twenty five Diagnosis Hypertension cardiac hypertrophy and myocardial failure Therapeutic result Improved respiration with relief from dyspnea disappearance of congestion at lung bases diuresis with loss of edema decrease in size and tenderness of liver Improved vital capacity Weight 59 Kg Digitalis 0.033 Gm per kilogram of body weight.

increased, the heart rate slowed but seven beats per minute The blood pressure fell 10 points from 145 during the control period rising later to 165 The evidence of therapeutic effect was further indicated by diuresis with loss of edema, relief of the dyspnea, decrease in the size and tenderness of the liver and in the disappearance of congestion of the lung bases, after a total of but 2 Gm of digitalis following a control period of five

days during which no digitalis or cardiac drug was given Figure 172 illustrates a very similar type of case characterized by an increase in diuresis, by a fall in blood pressure, decrease in

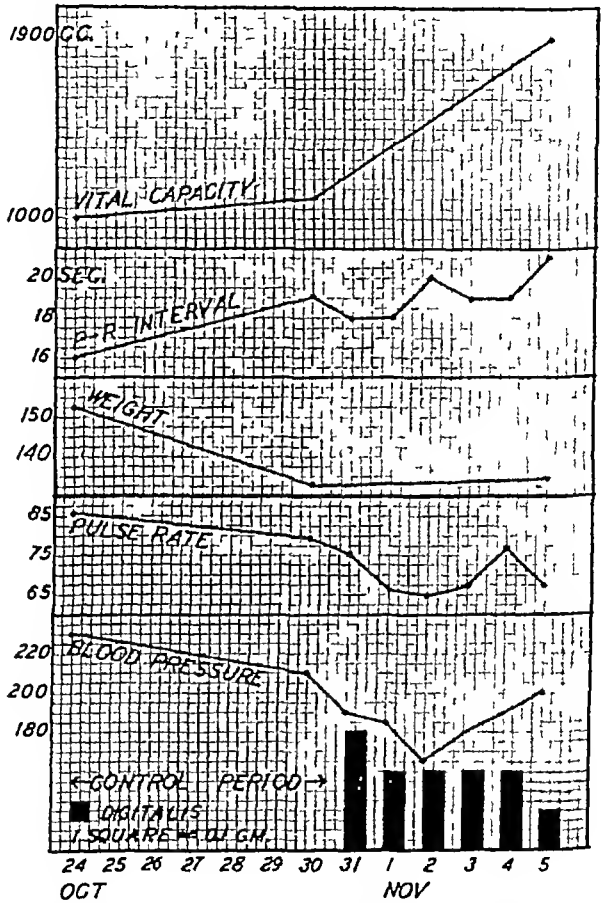


Fig 172.—I W, colored, male, age forty-seven Diagnosis Arteriosclerosis, hypertension and myocardial failure and right hydrothorax Therapeutic result Disappearance of Cheyne-Stokes respiration, dyspnea and orthopnea, diuresis with loss of edema and decrease in body weight Disappearance of rales in lungs, diminution in size of liver with loss of tenderness Weight, 59½ Kg Digitalis, 0 081 Gm per kilogram of body weight

weight, a disappearance of the cyanosis and edema and a decrease in the size and tenderness of the liver, without, however, any conspicuous change in the heart rate, a fairly typical

record It should be emphasized that we are giving merely the response to foxglove without allusion to the accompanying plan of control, our problem being a discussion only of the indications for its use In the instances illustrated by the accompanying charts a period of four to six days has preceded the administration of digitalis during which a rigidly controlled fluid intake and diet with the occasional use of a sedative, and routine catharsis, were the only remedial measures employed It, of course, very often happens that no such control period is possible and that one is obliged to give digitalis from the first We are indebted to Dr Martin's[16] clinical study, carried out on the wards of the hospital, for the illustrative cases

The occasional necessity for the possible emergency use of digitalis raises the question as to the desirable form of the drug under such circumstances In addition to the tincture and the powdered leaf, which constitute the preparations most frequently employed, we have strophanthin, a glucoside obtained from *Strophanthus Kombé*, available in the amorphous form or the crystalline ouabain (g Strophanthin) These may be given intravenously in doses of 0 5 or 0 3 mg respectively On rare occasions in the presence of acute cardiac dilatation with great venous engorgement and edema, the removal of 500 to 800 cc of blood from the arm vein followed by the injection of strophanthin through the same needle in wonderfully helpful and dramatic in the relief given In the period preceding the more modern studies of the action of digitalis upon the heart strophanthin was used much more frequently than is the custom today in many clinics Formerly the rapidity of the absorption of the digitalis preparations when given by mouth was not understood and it was often thought necessary to use intravenous therapy when administration by mouth would have accomplished the desired result, though less rapidly When given by mouth the effect of digitalis absorption may be noted in from four to six hours [19] Standardized preparations of digitalis for intramuscular use are also available.

In the treatment of cardiovascular hypertensive disease though there may be a difference of opinion, or of interpreta

tion, there is much clinical evidence that warrants the extended use of digitalis in perhaps smaller doses over longer periods of time Here Withering's early clinical observation is today as sound and as applicable as when first stated Referring to the apparent variation in the individual's susceptibility Withering says "in persons of tense fiber and great natural strength, with the body in Ascites, and the limbs in Anasarca, hard and resisting, it (Foxglove) seldom succeeded, whilst on the contrary if the pulse was found feeble or intermitting and the anasarcous limbs readily pitting on pressure the body soft and fluctuating the countenance pale and the skin cold, the diuretic qualities of the plant were to follow its use, in a kindly manner" Concisely put, the modern rendering of the above would be "of great value in certain conditions, notably auricular fibrillation, and in a selected group of cases with general edema" While the significance of the blood pressure measurements was, of course, unknown, it is implied in the first part of the quotation There can be no question, of course, as to the indications for its use in such cases when there is obvious cardiac failure We have never seen the blood pressure raised to any significant extent, more often the clinical improvement which follows its administration is succeeded by a fall in the blood pressure readings In the presence of a normal sinus rhythm, as stated, we do not expect any slowing in the heart rate, but we do assume that a more efficient systolic contraction may follow its use and there is abundant clinical evidence of its value in these cases Figure 172 illustrates a typical instance

It is also true that in certain of these hypertensive states, even in the absence of signs of myocardial failure, a continual use of digitalis over a long period in a so-called "maintenance dose" (0 1 to 0 2 Gm daily) often adds much to the subjective clinical comfort of the individual, in such instances without, of course, any objective indication of digitalis effect There would seem to be theoretically but little justification for its use under these conditions, but we firmly uphold the opinion that in these instances empiricism has justified the means to an end

It is apparent, then, that in the presence of high blood pres-

sures the most striking results of digitalis administration follow in the presence of extensive edema. So characteristic a result only further emphasizes the value of the drug in the presence of a normal sequential rhythm with edema

Acute Infections.—With the demonstration of the absorption and pharmacological effect of digitalis upon the myocardium in the presence of pneumonia, there followed a method of procedure which supported its use as a routine measure from the first in all cases of pneumonia It was subsequently shown that when digitalis was given during the course of the disease in a certain proportion of cases auricular fibrillation was prone to occur,[4] and it was further shown that in the condition of anoxemia experimentally produced auricular fibrillation could be more easily induced [21] With these facts available we have held the opinion that, in general, in the young adult with no cardiac history nothing was gained by the administration of digitalis in pneumonia In individuals of over forty with a definite cardiac history and obviously making "heavy weather" it may be given from the first, though in the writer's opinion of uncertain value under the circumstances We have seen complete heart block and a number of instances of transient auricular fibrillation follow digitalis therapy in pneumonia Though there is no doubt as to the drug's action upon the myocardium in such cases it is difficult to evaluate its effective influence for good In some carefully studied series the end results were surprisingly unsatisfactory[26] and there is a wide divergence of opinion among many internists of large experience as to its value under the conditions outlined In view of the fact that in most instances the drug is fairly rapidly absorbed—within four to six hours—the necessity for its administration early in pneumonia in individuals under forty, without a history of rheumatic fever, or without definite evidence of cardiac disease, seems unnecessary

In the presence of any nonspecific fever with its associated tachycardia there is seldom any indication justifying its use, and when given under these conditions there is usually little or no evidence of any clinical effect.

Paroxysmal Tachycardia—Among the disturbances of the cardiac mechanism the occurrence of a paroxysmal tachycardia is of itself no indication for digitalis Indeed it is conceivable that given early in the course of such an attack the drug may do harm When, however, such a tachycardia has persisted to the point of giving rise to signs of cardiac failure then the drug should be used for its direct effect to combat the cardiac dilatation that follows these wearing attacks of rapid rates of beating

With the tachycardia that sometimes follows during convalescence from typhoid fever or other infection, digitalis is, of course, contraindicated

Pulsus Alternans—The occurrence of a true pulsus alternans, always of grave prognosis, connotes a seriously involved myocardium In our judgment this is one of the definite indications for the use of digitalis, though theoretically in view of the nature of the disturbance and the extent of the myocardial damage its effect might be questioned By some clinicians the use of digitalis in such cases is considered to predispose to the occurrence of alternation We have, however, never seen pulsus alternans develop under conditions definitely attributable to digitalis therapy and consider its use under the circumstances of the greatest value [25]

Pericarditis with Effusion—There seldom arises any indication for the use of digitalis in the presence of pericarditis with effusion If, however, for any reason the drug is used under such conditions it should be given cautiously With any extensive effusion into the pericardium there is often a tendency for the occurrence of certain cardiac irregularities On more than one such occasion when digitalis has been used its exhibition was followed by similar disturbances With the greatly increased pressure within the pericardial sac there apparently follows a certain degree of myocardial anoxemia which seems to favor the occurrence of these irregularities We have encountered both auricular fibrillation and complete heart block in pericardial effusion apparently attributable to the drug

It is well known that the important treatment in these cases

is to remove the fluid and relieve the mechanical embarrassment. In certain other conditions represented by chronic pericarditis and pericardial mediastinitis, in so-called "Pick's disease" or in polyserositis the urgent necessity for digitalis often arises and it may be found to be of great value as an adjuvant of the other methods of treatment such as surgical interference to free the heart (cardiolysis)

Coronary Thrombosis—With the occurrence of a severe coronary occlusion the signs of acute circulatory collapse as evidenced by the feeble cardiac impulse, the poor quality of the heart sounds, the gallop rhythm, the fall in blood pressure, the cyanosis and the pulmonary edema, comprise a group of symptoms dramatically suggesting the need for digitalis as a part of the essential treatment, at least so interpreted by us

We must, however, frankly admit that in connection with the use of digitalis early in this condition, a wide difference of opinion prevails in the various medical clinics everywhere. There are, theoretically, two schools of practice, those who give digitalis early, and those who advise against its use at this stage This latter group would also, I believe, hesitate to advise its use in the absence of auricular fibrillation

It is a little difficult for the writer to understand the necessity for, or the wisdom of, such delay in many instances It is even said that the use of digitalis early in the course of such cases is "not wholly without danger" It is apparently assumed that there may be a certain risk of the formation of mural thrombi and that if the systolic contractions are too energetically increased an embolus may be dislodged On purely theoretical grounds we are warned against the irritable effects of the drug upon the myocardium and the depression of conductivity that may follow its use particularly when a part of the Purkinje system may be already damaged[11] Such assumptions, implying both an extraordinarily efficient and over vigorous response to the drug mechanically and to the effect of vagal stimulation from the doses commonly used, seems somewhat exaggerated It is, of course, perfectly conceivable that in the presence of extensive thinning of the ventricular wall

associated with a massive infarction rupture might occur, irrespective of the use of digitalis

We have used the drug in coronary thrombosis both early and late and have never seen the slightest untoward result follow its administration and have further been led to believe that it had been of value when given from the first No question can arise as to the propriety of its use in the later stages when auricular fibrillation is present—often with clinical edema

In this connection it is of interest that there is certain evidence that, in dogs at least, the production of experimental cardiac infarction by ligation of a coronary artery, is followed after a lapse of four days by a diminished tolerance to digitalis of from 20 to 30 per cent less than normal, and that from six weeks to six months after the experimental ligation, though the dog's tolerance to the drug had been somewhat regained, it was still slightly less than in normal animals The diminished tolerance was attributed to the extent of and to the stage of the infarcted area

Under analogous circumstances in man the writers warn against "massive doses" of digitalis, with which warning we agree We should never even suggest the use of massive doses in coronary thrombosis [1]

Cardiac Hypertrophy—With the use of digitalis as a preventive measure against the possible development of cardiac hypertrophy we have had no experience Based entirely upon the observations on rabbits in which it was shown that in a series of animals with experimental valvular lesions, to whom digitalis was given over a fairly long period, the hearts showed less enlargement and a better reserve capacity than in a similar series which had received no digitalis, the assumption was advanced that the foxglove actually retarded the cardiac hypertrophy and improved the heart's functional efficiency [3] Acting upon this idea it has been suggested that with evidences of beginning cardiac enlargement, in the absence even of other symptoms, digitalis should be given and particularly to individuals in the older age groups with slight breathlessness on

exertion In such cases small doses of digitalis are advised for continuous daily use [2]

Summary—We may summarize the substance of our impressions so briefly touched upon by emphasizing the extraordinary clinical value of digitalis when prescribed with a reasonable understanding of what may be expected from its use. Our evidence of its great value in clinical medicine is based upon the empirical experience of one hundred and fifty years, together with a vast array of experimental evidence upon animals and human beings since 1870 covering every phase of the pharmacology and chemistry of the drug Its chief value is found today in the treatment of auricular fibrillation and secondly in certain cases of cardiac failure associated with edema with and without associated arterial hypertension In the failure associated with valvular disease either of rheumatic, syphilitic or of arteriosclerotic origin it is extremely valuable, though a great difference in the clinical results and apparent clinical effect will be encountered It has been our experience that in the response to digitalis there is a distinct difference between rheumatic, syphilitic and arteriosclerotic cardiac disease When gauged by the relief from edema the arteriosclerotic hypertensive group shows the most satisfactory response, the rheumatic next, and lastly the syphilitic. This has been emphasized by many but is very graphically put by Marvin [17] As a cause of congestive heart failure with normal rhythm it is significant that cardiovascular hypertensive disease and cardiovascular syphilis are the two common agents while chronic pulmonary disease stands third in the list and is followed by chronic rheumatic heart disease [70]

It should be evident that digitalis is of no value whatsoever in controlling such irregularities of the rhythm as premature beats, or paroxysmal tachycardia or the tachycardia of infections It is of questionable value in pneumonia although there is considerable evidence supporting its use [4, 17] It is contraindicated in the preoperative stage of exophthalmic goiter when Lugol's solution acts as a specific remedy but may be used with the appearance of auricular fibrillation and signs

of cardiac failure In the so-called "postoperative surgical shock" digitalis is contraindicated except when definite signs of cardiac failure appear In conclusion may we add the statement that there is no condition of the myocardium excepting only the occurrence of pulsus alternans, which acts as a contraindication to surgical interference if such is necessary

BIBLIOGRAPHY

1 Bellet, S , Johnston, C G and Schechter, A B Arch Int Med., 54, 509, 1934
2 Christian, H A Jour Amer Med Assoc., 100, 789, 1933, and New England Jour Med , 208, 66, 1933
3 Cloetta, M Arch f exp Path u Pharm , 59, 209, 1908, and Jour Amer Med Assoc., 93, 1462, 1929
4 Cohn, A E , and Jamieson, R A Jour Exp Med , 25, 65, 1917
5 Cohn, A E , and Steele, J M Jour Clin Invest., 11, 871, 1932
6 Cohn, A E , and Stewart, H J Jour Clin Invest , 1, 97, 1924, 6, 53, 1928, 6, 79, 1928, and 11, 897, 1932
7 Cushny, A R Jour Pharmacol and Exp Therap., 11, 103, 1918
8 Cushny, A R , and Edwards, C W Amer Jour Med Sci , 133, 66, 1907
9 Eggleston, C Arch Int Med., 16, 1, 1915
10 Eggleston, C Amer Jour Med Sci , 140, 625, 1920
11 Kilgore, E S Jour Amer Med Assoc , 100, 315, 1933
12 Lewis, T , Drury, S N , Wedd, A M , and Iliescu, C Heart, 9, 207, 1921–22
13 Levy, R L Arch Int Med , 32, 359, 1923
14 Levy, R L , Bruenn, H G , and Ellis, S S Amer Heart Jour , 8, 226, 1932
15 Mackenzie, Sir J Brit Med Jour , 1, 587, 702 and 759, 1905, Heart, 2, 273, 1911–1912
16 Martin, L E Jour Clin Pharm and Exp Therap , 31, 229, 1927
17 Marvin, H M Jour Clin Invest , 3, 521, 1927
18 McEachern, D , and Baker, B M , Jr Amer Jour Med Sci , 183, 35, 1932
19 Pardee, H E B . Jour Amer Med Assoc , 75, 1258, 1920
20 Parkinson, J., and Clark-Kennedy, A E Quart Jour Med , 19, 113, 1926
21 Resnik, W H Jour Clin Invest , 2, 125, 1925
22 Ritchie, W T Auricular Flutter, 1914, W Green and Son, Edinburgh and London
23 Robinson, G C , and Wilson, F N Jour Pharm and Exp Therap , 10, 491, 1918
24 Wedd, A M Bull Johns Hopkins Hosp , 30, 131, 1919
25 Windle J D Quart Jour Med., 10, 274, 1917
26 Wyckoff, J , Du Bois, E F , and Woodruff, I O Jour Amer Med Assoc., 95, 1243, 1930

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR T B FUTCHER

FROM THE MEDICAL SERVICE OF THE JOHNS HOPKINS HOSPITAL

DIAGNOSIS AND TREATMENT OF DIABETES INSIPIDUS

Definition—In 1794 Johann Peter Frank[1] described diabetes insipidus as "a long-continued abnormally increased secretion of nonsaccharine urine which is not caused by a diseased condition of the kidneys" A better definition could not be devised for the present day

Etiology—No one familiar with the literature and the experimental work that has been done with the endeavor to throw light on the cause of this comparatively rare disease will admit that all the problems concerning its etiology have yet been solved Although much experimental work was done in the latter half of the last century, particularly by Eckhard and Kahler, it must be admitted that these experiments, in which lesions were produced in various parts of the central nervous system of animals, added very little to our knowledge of the cause of persistent polyuria

In the last two and a half decades, however, as a result of experimental work and the careful investigation of cases that have come to operation or autopsy, we can definitely assert that in the vast majority of cases of diabetes insipidus the disease is due to some lesion involving the posterior lobe of the hypophysis or of the hypothalamic region at the base of the brain

Since 1910, three conceptions have in succession been entertained concerning its etiology

1 That it is caused by disturbed function of the posterior lobe of the hypophysis

2 That it is produced by organic changes involving one or more of the structures comprising the hypothalamus

3 That there is a center, the *nucleus supraopticus* or *nucleus paraventricularis*, located in the hypothalamus near the floor of the third ventricle on each side of the brain, that presides over normal water metabolism, that nerve fibers extend from the cells of this center and pass down through the hypothalamus and infundibular stalk and spread throughout the entire posterior lobe of the hypophysis and even between the cells of the pars intermedia, and that a lesion involving any part of this tract, the *tractus supraoptico-hypophyseus*, may so disturb water metabolism that diabetes insipidus results

With the limited time at our disposal only a very brief summary of the evidence supporting these various conceptions can be given Although it was not until 1910 that the possible relationship between the disease and the hypophysis was pointed out by Cushing, yet Rowntree[2] states that as far back as 1883 Hagenbach[3] reported a case of diabetes insipidus in a girl four years of age, who had tuberculous meningitis and a caseous nodule involving the infundibulum Hagenbach, however, gives no intimation that he appreciated the importance of this infundibular lesion as the possible etiology of the diabetes In 1910, Cushing[4] observed a transitory glycosuria following posterior lobe hypophysectomy in dogs In 1913, he reported that in his first 100 cases of pituitary disease polyuria had been so marked that it had led to a diagnosis of diabetes insipidus by the physicians referring the patients The first clinical observation showing a possible relationship between the disease and lesions of the hypophysis was made by E Frank[5] in 1912 He reported a case in a man who had been shot and *x*-rays revealed the fact that the bullet was lodged in the sella turcica In the following year, 1913, M Simmonds[6] reported in a woman, aged thirty-seven, two months after an excision of the breast for carcinoma, a marked polyuria and polydipsia The autopsy showed, in addition to numerous other metastases, one involving and destroying the posterior

thalamus In 1922, Lhermitte reported a case in which a syphilitic lesion involved both the tuber cinereum and the infundibulum In 1925, Babonnex and Lhermitte described another case of diabetes insipidus in which there was syphilitic involvement of these same two parts of the hypothalamus in association with a syphilitic basilar meningitis The writer,[12] in 1929, reported the disease in a patient with a carcinomatous metastasis of the hypothalamus involving the tuber cinereum, the primary growth being a bronchogenic carcinoma of the lung The literature contains other cases in which the disease accompanied hypothalamic lesions without any apparent involvement of the posterior pituitary lobe

It will thus be seen that there is rather strong clinical evidence, dating from Erdheim's observations in 1904, and from the experimental work on animals subsequently, that diabetes insipidus can be produced, and may possibly be only produced, by lesions of the hypothalamus

From the foregoing it will be seen that we have the hypophysis and the hypothalamus proponents of the cause of diabetes insipidus It now remains to refer very briefly to later work which tends to show that the adherents of both views may be right in their interpretation This concerns the important work of Pines[13] in 1925 and of Greving[14] in 1926 These observers believe that there is a water-regulating center on each side of the brain near the floor of the third ventricle, which is called the *nucleus supraopticus* or *nucleus paraventricularis* From the multipolar cells constituting this center they find that nonmyelinated nerve fibers extend down through the hypothalamus near the tuber cinereum and pass through the infundibular stalk into the posterior pituitary lobe, where they weave themselves in a "basket-like" fashion around what appear to be secretory islands This path is called the *tractus supraoptico-hypophyseus*

Knowing the effect that extract of the posterior pituitary lobe has on the urinary output, if we accept the view that there is a water-regulating center, the nucleus supraopticus, it is possible to conceive that the function of such a center might be-

come impaired by any disease of the posterior lobe diminishing or abolishing the secretion of pituitrin, especially as Pines and Greving have shown the nerve connection between the center and the posterior lobe the tractus supraoptico-hypophyseus We can conjecture that it may be found that tumors or other lesions involving the nucleus supraopticus, the posterior hypophysial lobe, or the tract anywhere between these points may produce diabetes insipidus

We now know that symptoms of transitory diabetes in sipidus follow epidemic encephalitis lethargica and it is easy to conceive that the water regulating center or some part of the tractus supraoptico-hypophyseus could be involved in the focal lesions In a similar way, the cases of diabetes insipidus accompanying cranial fractures, tumors, actinomycosis, tuberculosis and syphilis may be explained In the same way may also be explained the cases of diabetes insipidus the neurological surgeons so frequently find following supracellar decompressions and operations on tumors at the base of the brain

The consensus of opinion at the present time is that practically all cases of diabetes insipidus are due to some lesion involving either the hypothalamic region or the posterior pituitary lobe It is rather difficult to explain the comparatively rare instances in which heredity plays a part. Weil[15] reported a family in which among 90 members in four generations 25 exhibited persistent polyuria without any manifest deterioration in health One naturally wonders whether in these cases any inherited defect in the hypothalamus or posterior pituitary lobe could be transmitted

Diagnosis—It has been the usual custom to divide the cases of diabetes insipidus clinically into two groups

1 Primary or idiopathic, in which no recognizable organic lesion can be discovered The hereditary group might belong here

2 Secondary or symptomatic, in which some evidence of a demonstrable organic lesion can be discovered.

It is doubtful whether such classification is any longer tenable Knowing as we do that the vast majority, if not all the

cases, are due to lesions either in the hypothalamus or the posterior pituitary lobe, one must always keep in mind the possibility that the cases in the primary or idiopathic group are really due to lesions at the base of the brain, but that at the time the cases come under observation the evidences of pressure or neighborhood symptoms have not reached the stage where they are recognizable, yet may do so at a later date

From a diagnostic standpoint the outstanding symptoms of diabetes insipidus are the marked, persistent polyuria and polydipsia The amount of urine passed may be enormous Usually it ranges between 8 and 12 liters, but may reach the enormous output of 43 liters in the twenty-four hours as in one of Trousseau's cases, the largest amount on record The quantity of fluid ingested is correspondingly large Many investigations have been carried out to endeavor to ascertain which is primary, the polyuria or the polydipsia, with contrary opinions Ebstein and Nothnagel held that the condition is a primary polydipsia Recent experimental work on rats by Richter[16] seems to show convincing evidence that the polyuria is primary The urine is extremely pale, of very low specific gravity, 1 000 to 1 005, free from glucose but may contain traces of inosite or muscle sugar, probably resulting from the flushing out of muscles by the enormous amount of water passing through them Albumin may be present at times in minute traces, although the usual statement is that it is absent. Its occasional presence in a case may be a complicating factor in diagnosis Rowntree states that in the Rochester series 16 of the 24 cases showed traces of albumin at some period of their study

Owing to the fact that so many of the cases of diabetes insipidus are secondary to lesions of the hypothalamus or hypophysis, it is not surprising that the victims frequently show cerebral manifestations, and these should be most carefully searched for in every case Typical pituitary syndromes may be present There may be choking of the disks or restrictions of the fields of vision Ocular palsies, particularly of the sixth nerve, may be present Intermittent bitemporal hemianopsia

may occur, particularly in the cases associated with basilar syphilitic meningitis, as was emphasized by Oppenheim From tumor pressure the acuity of vision may progressively fail Severe headaches and vomiting may occur The knee jerks are nearly always markedly increased

The pulse and blood pressure are normal The heart is not enlarged, notwithstanding the increased amount of water that has to be transported The blood count shows no consistent changes A positive blood Wassermann with evidences of basilar brain symptoms should strongly suggest the existence of a gumma in the hypothalamus, with or without a basilar luetic meningitis

There are a number of affections, accompanied by polyuria, the features of which may simulate those of diabetes insipidus, but with careful study there should be no difficulty in making a differential diagnosis Highly neurotic men and women not infrequently have a marked polyuria, but this is usually transitory or intermittent and will usually disappear by eliminating the cause of the patient's nerve strain or by administering a course of nerve sedatives, such as bromides Hysterical polyurias are not uncommon but yield to appropriate treatment.

The thirst and polyuria of diabetes mellitus are readily recognized by the urinalysis and blood sugar studies

Chronic interstitial nephritis is the disease which may give rise to the greatest difficulty in diagnosis Here 3 to 5 liters of very pale urine of low specific gravity and with the merest traces of albumin may be passed in the twenty four hours The fact that some cases of diabetes insipidus have intermittent traces of albumin in the urine adds somewhat to the confusion However, careful study should lead to no difficulty in making a differential diagnosis The interstitial nephritis cases will nearly always show hyaline casts, which are practically never found in diabetes insipidus The finding of hypertension, enlarged heart, low phenolsulphonphthalein excretion and high nonprotein blood nitrogen and kreatinin should really lead to

no difficulty in deciding that one is dealing with a case of chronic interstitial nephritis

Where there is any question of doubt in the differential diagnosis between diabetes insipidus and the various conditions simulating it, the application of the therapeutic test by the injection of pituitrin is a valuable aid A resultant amelioration of polydipsia and polyuria following this procedure would strongly point toward the former It must be remembered, however, that some cases of diabetes insipidus do not respond to pituitrin treatment

Treatment—Previous to 1913 one is impressed with the enormous number of remedies mentioned in textbooks for the relief of the distressing thirst and polyuria in this disease The large number advocated is a clear evidence of their inefficiency Opium, valerian, and ergot seem to have been the most popular remedies

Since the discovery in 1913 by von den Velden and Farini that pituitrin had a striking effect in reducing the polyuria and polydipsia, posterior pituitary lobe preparations have come into general use and have proved strikingly effective in relieving these symptoms in many of the cases Following the work of Schafer and his colleagues, Herring and Magnus, in 1906, which revealed the fact that the posterior pituitary lobe hormone had a pronounced effect on urinary excretion, many researches have since been carried out by physiologists, pharmacologists and clinicians with the view of throwing clearer light on how this hormone influences urinary excretion Time will not permit a complete review of these studies In a research reported by Nelson and Woods[17] in 1933, from the Pharmacological Laboratory of the University of Michigan, these investigators state that the current views are that the effect of posterior pituitary lobe extracts on urinary excretion is represented as occurring in three phases After injection of the preparation there is first a primary anuria, due possibly to a spasm of the ureters, this is followed promptly by a brief diuretic effect associated with marked increase in chloride excretion, and finally a more lasting antidiuretic effect The

factor that concerns us is the marked antidiuretic action of the extract, which is its dominant effect. The mechanism by which this antidiuretic action is produced has not yet been definitely settled

The posterior pituitary lobe preparation that has been most frequently used in the treatment of diabetes insipidus is commercial pituitrin When effectual the results are most striking In many cases an output of 8 to 14 or more liters of urine in the twenty-four hours is reduced to about the normal limits, with a corresponding reduction in the polydipsia The patients are often strikingly relieved of their disturbed nights resulting from their craving for water and frequent voiding

Any good preparation of pituitrin may be used (Parke, Davis and Company put it up in 1-cc ampules in two strengths, the obstetrical and surgical, the latter being twice as potent as the former) It is administered hypodermically The dosage depends upon the individual case In mild cases 0 5 to 1 cc. of the obstetrical preparation twice daily may be sufficient I, personally, have usually used surgical pituitrin in the doses noted above The number of doses required in the twenty four hours varies A dose of 0 5 to 1 cc. of surgical pituitrin should be given the patient before retiring, so as to make their nights more comfortable. Usually another dose is required in the morning The antidiuretic effect of a dose usually does not last more than four to six hours The administration of pituitrin may not be without its unpleasant effects It may produce local reactions, and, not infrequently, produces intestinal cramps owing to its effect on smooth muscle fibers. In such cases Barker has suggested the use of smaller doses at more frequent intervals

Most patients naturally object to the subcutaneous administration of the drug Blumgart has found that the nasal administration of pituitrin is sometimes effective A tampon of cotton soaked with 0 5 to 1 cc. may be inserted into one nostril two or three times daily, or 1 cc of surgical pituitrin may be diluted with 30 cc of normal salt solution and the patient instructed to spray this into each nostril several times

daily I have seen one case in which this procedure was very helpful, whereas the subcutaneous method had very little effect

Other posterior pituitary preparations have been used In 1934, Smith[18] reported two cases with very satisfactory results in which a very finely powdered posterior pituitary lobe extract was blown into the anterior and upper part of each nasal cavity

Reference here should be made to the possible influence of "intermedin," the hormone of the pars intermedia isolated by Zondek[19] in 1932, on the urinary output in diabetes insipidus, and the possibility that this disease may be dependent on disturbed function of the intermediate lobe Zondek and his collaborators demonstrated intermedin to be present in the entire pituitary gland, in the infundibular stalk, and in the walls of the third ventricle Sulzberger[20] secured some intermedin from Zondek, and, in a preliminary report, claims to have found that it had a quite potent effect in reducing the polyuria in two cases of diabetes insipidus in which it was used Considering the statement that intermedin is found in all parts of the pituitary, the possibility that the beneficial effect of pituitrin in the treatment of this disease might be due to contained intermedin has, at least, to be entertained

In this connection it should also be recorded that Russell S Ferguson[21] and his associates have isolated from a crude extract of the middle pituitary lobe a preparation which they call "aquamedin " They found this preparation to be very effective in the treatment of ten cases of diabetes insipidus, and they believe that it specifically controls the water balance of the body

Recognizing the possibility that there may be a water-regulating tract in the hypothalamus and posterior pituitary lobe and that pituitrin is sometimes ineffective, Elmer, Kedzierski and Scheps[22] have proposed a classification of diabetes insipidus from an etiologic and therapeutic standpoint It is as follows

(*a*) Cases due to destruction of the posterior lobe of the hypophysis Here the posterior lobe hormone, being absent or diminished, fails entirely or only in part to sensitize the regu-

latory centers for water and salt in the hypothalamus In these cases pituitrin has a definite, though transitory therapeutic effect, because the regulatory centers in the hypothalamus are intact.

(*b*) Cases due to destruction of the water- and salt regulatory centers in the hypothalamus In these the secretion of the posterior lobe is still produced, but it cannot sensitize the hypothalamic centers because they are destroyed In this group the pituitrin has no effect whatever, since the regulatory centers in the hypothalamus are destroyed and are incapable of sensitization

(*c*) Cases in which there is an interruption of the communicating nerve fibers connecting the hypothalamus and the posterior lobe of the hypophysis This group, they state, is insufficiently understood and requires further investigation The therapeutic effect of pituitrin is not stated

If the views of these authors be correct, the failure of pituitrin to be effective therapeutically in some patients may represent those cases in which the so-called "water regulating" center or centers are destroyed

In this disease long-continued or permanent treatment is necessary unless the etiologic factor is removed, as the administration of pituitrin constitutes only a form of substitution therapy Commercial posterior pituitary lobe preparations by oral administration have, up to the present time, proved ineffective.

Herrick[3] reported a case in which there were beneficial effects following lumbar puncture It must be emphasized, however, that certain risks attend this procedure in basilar brain tumors

Where syphilis occurs antiluetic treatment should be instituted, for there may be gummatous or other basilar luetic lesions causing the disease Four of nine cases Ia[4] reported in 1904 seemed undoubtedly to have had lues Antiluetic treatment by iodides and mercury then in use had a beneficial effect on the general health of the patients but did not materially

influence the polyuria Modern treatment is likely to be more effective

Several cases of diabetes insipidus have been found in association with actinomycotic lesions at the base of the brain Where the ray fungus has been demonstrated in lesions elsewhere, iodide of potassium should be administered Some recorded cases have shown at least temporary benefit from the standpoint of the diabetic symptoms

Eric Meyer claimed that he obtained beneficial results from the use of theocin He held that it tended to increase the ability of the kidneys to concentrate urine, thereby enhancing the elimination of solids in the urine The dose is 0 2 Gm (3 grains) three times daily

The dietary treatment plays a small rôle Moderate restriction of the water intake is admissible, but this must not be overdone Meyer advised a certain reduction of salt and protein, but, as it has been shown that the kidneys are capable of concentrating urine, this restriction does not appear to be necessary

Cases showing clinical evidences of tumors involving the pituitary or midbrain should be treated on general surgical lines irrespective of the existence of diabetes insipidus Surgical interference may preserve the vision and relieve the victims of some of the subjective symptoms dependent upon increased intracranial pressure Surgical measures apparently rarely help the diabetic features, and we are familiar with the fact that transitory diabetes insipidus not infrequently follows operation for basilar brain tumors

SUMMARY

1 Most cases of diabetes insipidus are due to lesions at the base of the brain involving the hypothalamus or posterior lobe of the hypophysis There is rather convincing evidence that the essential cause of the disease is some lesion involving the structures comprising the hypothalamus Pines, Greving and others are of the opinion that there is a water-regulating center, the nucleus supraopticus or nucleus paraventricularis,

on each side of the brain near the floor of the third ventricle, with nerve fibers passing from the cells of this center down through the hypothalamus and infundibular stalk and spreading out throughout the posterior pituitary lobe, surrounding islands of secretory cells The tract is called the tractus supraoptico-hypophyseus Some competent observers are of the opinion that diabetes insipidus may be induced by lesions that involve any part of this tract Experience may eventually show that there are no so-called "primary" or idiopathic cases of the disease. It is possible that such cases come under observation at a stage where there are no recognizable neighborhood symptoms of organic lesions at the base of the brain

2 The most effective therapeutic treatment is the administration of posterior pituitary lobe preparations Intermedin and aquamedin from the pars intermedia, apparently have also been shown to be efficacious

3 Cases due to syphilis or actinomycosis should have appropriate treatment

4 Surgical measures should be carried out in those cases with manifestations of a basilar brain lesion indicating neighborhood effects and increased intracranial pressure.

BIBLIOGRAPHY

1 Frank Johann Peter De Curandis Hominum Morbis Epitome etc., Lib V 1 94
Rowntree L G Oxford Medicine Vol I Part I p 1 9
3 Hagenbach F Jahrb f Kinderh Leipzig 1883 n F, 19 214
4 Cushing Harvey Bull Johns Hopkins Hosp., 21 127–169 1910
5 Frank E Berl Klin Wchnschr 1917 49 393
6 Simmonds M Munchen med Wchnschr., 1913 168 901
Von den Velden R Berl Klin Wchnschr., 1913 50, 2033
8 Farini A Gazz d osp Milano 1913 34 8 9 and Clin Med Ital., Milano 1913 52 497
9 Camus and Roussy Compt. rend Soc Biol., 1913 75 453
10 Camus and Roussy Compt rend Soc. Biol., 19 0 83 15 8
11 Bailey Percival, and Bremer Frederick Arch Int. Med., 1921 8, 7
12 Futcher T B Am Jour Med Sci 19 9 8 83
13 Pines I L Ztschr f d ges Neurol u Psychiat., 1925 100 173–178
14 Crevinx R Deutsch Ztschr f Nervenh., 19 6 89 1 9–195
15 Weil A Virchow's Arch., 1884 95 0
16 Richter Curt P To be published in the near future

17 Nelson, Erwin E , and Woods, G G Jour Pharm and Exper Therap , 50, 1934, 241,
18 Smith, Francis M Jour Amer Med Assoc , 1934, 102, 660
19 Zondek, Bernard, and Krohn, Hans Klin Wchnschr , 11th Jahrg , 1932, 405–408, 849–853, 1293–1298
20 Sulzberger, Marion B Jour Amer Med Assoc , 1933, 102, 1928
21 Ferguson, Russell S Reported before the Cleveland Meeting of the Amer Med Assoc , 1934 Paper not yet published
22 Elmer, A W , Kedzierski, J , and Scheps, M Wien klin Wchnschr., 1928, 41, 591
23 Herrick, J B Arch Int Med , 1912, 10, 1
24 Futcher, T B Trans Ass Am Phys , 1904, 19, 247

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DRS JULIUS FRIEDENWALD AND SAMUEL MORRISON

FROM THE GASTRO-ENTEROLOGICAL CLINIC OF THE DEPARTMENT OF MEDICINE, UNIVERSITY OF MARYLAND

VALUE, INDICATIONS, LIMITATIONS AND TECHNIC OF COLONIC IRRIGATION

Introduction.—The history of enemata, of which colonic irrigation in its true sense may be looked upon as a modern modification, illustrates strikingly the changing attitude of the medical profession regarding its value as a therapeutic procedure. There is every indication when one reviews the history of enemata and irrigations that the former is an ancient procedure (although the administration of the enema as it is known to us at present has been attributed to Marco Gatemaria who died in 1496) while the latter is not clearly described until more modern times. Montague is confident that we can trace through the history of ancient Egypt up to the doors of prehistoric times a very certain knowledge of the principles involved in the enema. In the 17th and 18th centuries the clyster had reached the height of its popularity and reigned as one of the few outstanding measures for combating disease. It was soon practiced as a fad but toward the end of the 18th century serious thought was given to its application and limitations. At that time a number of modifications were made in the mechanical construction of clyster syringes, the clyster chair was introduced and a number of compact portable instruments were devised. Somewhat later the gravity irrigator was introduced, as a result a greater quantity of liquid could be utilized and the pressure varied as desired. When the "fountain syringe,"

as it was called, replaced to a certain degree the older methods in the 19th century, the introduction of a great variety of laxative pills was soon accompanied by a relative waning of interest in the clyster Although Russell and others trace the use of colonic irrigation in its cruder forms to early times the form of colonic irrigation which today is a part of what has been termed physical medicine is evidently a distinctly modern procedure This is associated today, as it was in earlier centuries, with a reaction against laxative therapy with its tendency to produce colon irritation for it was soon observed that clyster treatment appeared to be a much more rational and soothing procedure Moreover, it was evident that if chronic constipation was present in so many of these cases of intestinal dysfunction, colonic irrigation, as a modification of the enema, was a more thorough therapeutic procedure than the latter and yet of the same nature In a strict sense the idea of intestinal irrigation separated itself from the enema confusion toward the latter part of the 19th century, notwithstanding the knowledge of it before that period

Throughout the development of this form of physical therapy a distinction is made between single washings of the lower bowel (enema) and repeated flushings of the entire colon with large quantities of clear or medicated fluids The latter is actually a colonic irrigation while the former, an injection of fluid into the lower bowel, and particularly below the pelvirectal flexure, is a distinctly different procedure and is classified as an enema The application of colonic irrigations was given its modern impetus by Doctor de Langenhagen of Plombieres in 1898 He introduced there a new apparatus which was referred to as the "douche horizontale" As Russell writes, "the term irrigation describes more accurately than the words clyster or enema, the treatment which is administered with the modern apparatus These methods lavage and thoroughly cleanse the walls, remove abnormal mucus and also empty the bowel The tone of the colonic muscles is improved and the blood supply augmented" The Plombieres method served as a somewhat original procedure which was followed later by many varia-

tions and it is interesting that only recently (1932) the approval of the Council on Physical Therapy of the American Medical Association was sought for a large number of new colonic irrigation devices

Value.—Colon irrigation, correctly employed, has definite therapeutic value. Very often the profession's prejudice against the procedure is based upon the ubiquity of its application as well as the perfectly unbelievable cures which are said to follow its use. However, some of the colonic lavage apparatus are so elaborate that they doubtless carry with them a psychotherapy often far more effectual than any antineurotic measure which could be employed. The physician who utilizes this method only occasionally should understand that its field of application differs from that of an enema which is given primarily to secure bowel evacuation (that is, left colon evacuation). A colonic irrigation, on the other hand, attempts to reach beyond the splenic flexure, *i. e.*, the usual defecation area, its field of activity, as its name implies, is the entire colon. Repeated washings may be required to eradicate an area of infection or to remove some thick, tenacious mucus or putrefying contents of the colon. Often the last few inches of the ileum may, by relaxation of the ileocolic sphincter, be irrigated at the same time. The value of the irrigation depends likewise on the frequency of its use which in turn must be governed by the existing disease process. For ordinary mucous colitis, putrefaction or focal infection cases Bastedo recommends the irrigation two or three times weekly at first, then every five days, then once a week. He employs irrigations oftener only in acute cases of other types and cautions that the introduction of water or other liquids into the bowel, whether as an enema or irrigation is an abnormal procedure, and cleaning out the whole colon too frequently may harmfully interrupt its normal functions.

A survey of the treatment of colonic affections with colonic irrigation has led us to the conclusion that the procedure as usually employed should, to say the least, not be encouraged. The harmful effects are frequently due to the habitual use of a measure which has been demonstrated experimentally to pro

duce irritation of the bowel Nevertheless, the regulated use of the procedure in certain cases is of definite benefit In our experience it has been observed that as a general rule, its use once or twice weekly for several weeks followed by a frequency of once in two weeks until the desired effect is produced, has usually met with gratifying results Our plan is to precede the irrigation, for which we use plain water, normal salt solution or bicarbonate of soda solution, by a cleansing enema We have found that irrigations are especially helpful in colonic conditions associated with functional intestinal stasis in which fermentation is a prominent feature and also in mucous colitis In ulcerative colitis our results have not been very encouraging except occasionally, in this condition the irrigations, if used at all, should be given extremely cautiously and in very small quantities When astringents and antiseptics, such as nitrate of silver, argyrol, tannic acid, permanganate of potash, acriflavin, gentian violet and mercurochrome are used, the proper dilution is an essential therapeutic factor, warm-water irrigations should follow these medicated procedures Very often the simplest irrigation solution is the most valuable, a fact which De Graaf commented upon many years ago Notwithstanding the general agreement against the use of so many solutions and elaborate formulae, they continue to be employed and multiply until they are as legion as the cures that are supposed to follow

It becomes clear that colonic irrigations are valuable from a psychic point of view as well as through their mechanical effects in aiding elimination and in cleansing the colon mucous membrane of abnormal mucus, infection, débris and foreign bodies (especially chemicals and fermentative and putrefactive products of digestion)

Irrigations are also of value in cases of atony because when given cold they stimulate peristalsis while, on the other hand, in spastic states warm solutions will produce relaxation of bowel musculature What the general effects of these local changes in temperature may be are not easily interpreted and the tendency to attribute every improvement which occurs concomitantly with colonic irrigation to its employment has probably

led to some of the unwarranted and debatable statements made regarding its value and efficacy It has been stated that cases of so-called "appendicitis" have been cured by this method or by using a modified technic (the cecal tube), but so-called "appendicitis" is such a vague condition in itself that a discussion of this and similar subjects can only deal in uncertainties If, however, the so-called "appendix attack" is in reality a condition of acute food poisoning or, in other words, of intestinal food allergy, the good effect of irrigation may be more easily understandable The same rationale of irrigation treatment may be applied to chronic poisoning due to various metals of which lead is a prominent example. Early use of colonic irrigation is apparently a thoroughly reliable procedure in these instances Similarly, certain cases of drug addiction may be aided especially during the time of withdrawal of the drug for at this period intestinal symptoms such as intense diarrhea can be controlled to varying degrees by the procedure

Diarrheas of bacillary, parasitic and nonspecific origins may also at times be aided by Irrigations Colonic irrigation has been employed to obtain upper colon contents in suspected parasitic infections, it has also been used as a therapeutic measure in the treatment of these infections by including specific drugs in the irrigation

There has always been and there will, in all probability continue to be considerable discussion pro and con concerning the use of colonic irrigation in the treatment of so-called "intestinal toxemia" associated with constipation There are arguments perhaps equally good in favor of and against the measure Obviously constipation can be relieved, at least temporarily and if a condition of intestinal intoxication exists it may seem to disappear judging from the patient's subjective feelings On the other hand, constipation can be relieved by simple measures in most instances and "intestinal intoxication" is explainable in other ways than as a result of constipation for in many instances the symptoms of this condition can be relieved, although the constipation continues to exist. It is interesting that the symptoms of what has been termed "auto intoxication"

can be produced by merely distending the rectum with some foreign body The whole problem becomes less controversial when the physician considers each case individually instead of subjecting all to the same routine therapeutic procedure without a complete objective examination It is fair to conclude that irrigation should be considered an auxiliary measure and not as a system of therapy in itself To attribute resumption of tone in an atonic bowel, for example, to colonic irrigation when a general upbuilding regimen is being followed is neither rational nor convincing For the same reason it is not worthwhile to discuss the infinite number of gastro-intestinal and general ailments which have been reported at one time or another with more or less enthusiasm as cured by irrigations through its general, local or reflex effects Often the more elaborate the technic, and the apparatus, the greater the percentage of reported "cures" Nevertheless, when applied within its limits the method is indeed valuable, but there should be a clear indication for its use and the importance of irrigation in the general plan of treatment must be held clearly in mind

Indications—Cold water by irrigation is obviously a tonic measure with certain exceptions On the other hand, warm irrigations are soothing and relaxing These are principles of hydrotherapy and dictate the use of the former in atonic states and the latter in spastic conditions of the bowel As a matter of fact it is recognized that the same measures are useful in producing general stimulation and relaxation It would seem that since general baths at regulated temperatures are simpler and of established benefit, the intestinal bath would not be indicated so frequently in that group of cases in which only the general effects of heat and cold are desired

In the dyschezia type of constipation the use of enemata and irrigations seems rational for it is well established that oral administration of laxatives in this condition is harmful However, dietary measures as well as treatment directed to any anorectal or lower colon disease which may be responsible for the retention-en-masse of fecal matter, is essential before its correction may be expected

There seems to be considerable diversity of opinion regarding the efficacy of colonic irrigations in constipation Hirschman, on the one hand, maintains that "quantities of fluid are a poor substitute for solid material on which the bowel muscle should contract. Regular irrigations by washing out the mucus, irritate the mucous membrane and rob the intestinal muscle of the normal stimulus for normal defecation Constipation or obstipation can never be cured by enemas or bowel flushes" On the other hand, Russell writes that "many practitioners find it difficult to understand how these methods of colonic irrigation can frequently cure constipation It is not sufficiently realized what an important part exercise plays in the proper function of the large bowel, and how insensitive the defecation reflex can become, and conversely, what a beneficial effect can be produced by a treatment which produces an average of sixty evacuations of the bowel each time it is applied—the defecation reflex being brought into action during a single irrigation as often as normally in two months of ordinary life This intensive stimulation reeducates the bowel, increases the blood supply and improves the tone of the muscles" We, as well as others, have been able to demonstrate bowel irritation following repeated colonic irrigations and we have often wondered whether some of the increased tone following irrigation was a result of the temporary hyperirritable condition produced by this procedure On the other hand, such irritable states are not of long duration when the irrigation is properly performed In our opinion the keynote to success in the treatment of constipation depends not so much on the colonic irrigation as upon the general therapeutic plan of which the irrigation may be a more or less important part depending upon the type of constipation and the individual in whom it has occurred It seems that within limits colonic calisthenics, using the method of irrigation, may have a tonic effect in certain instances, more often temporary, however, than lasting, depending largely on the associated treatment In some cases the tonic effect of the irrigation may be all important and actually curative, this, too, would depend to a great extent upon the type of previous treat

ment, the patient and the associated therapy Finally it may be concluded that the measure is definitely indicated in certain cases of constipation but it should not by any means be made a routine procedure

Whether colonic irrigations produce beneficial effects on certain other mucous and serous membranes in the body is difficult to prove To base such a conclusion on the reports of patients whose sinusitis or nasopharyngitis has improved during the irrigation treatment is more likely a coincidence than a relationship of cause and effect The impression has been gained by many that the various arthritides have been benefited by colonic irrigation as the result of overcoming intestinal stasis and in such instances it has been claimed that the focus of infection must have been located in the bowel It is, however, difficult to accept these conclusions since the improvement observed seems more rationally explained as the result of natural healing processes, or of concomitant therapeutic measures Furthermore, local and general measures in this group of disorders are distinctly more valuable and rational than colonic irrigations

Colonic irrigations are indicated for the removal of abnormal mucus, toxic products and bacteria from the bowel In other words, they are useful in many of those intestinal diseases in which irritation and infection are present To omit or even condemn the use of colonic irrigations in their entirety as a therapeutic procedure is unwarranted If a study of the material obtained by irrigation is used as a guide for the continuation of treatment many of the untoward reactions and poor results obtained by the procedure may be avoided Perhaps the employment of this measure without proper supervision and study is its greatest single objection One should remember that the colon absorbs fluids (*e g*, it changes the liquid material received from the small intestine to solid material), in this process the passage of bowel contents is retarded until absorption of selected material is completed If, during this normal activity, the process is prolonged or some other dysfunction occurs, an attempt should be made to bring about resumption of

normal motor activity and as a direct and immediate measure colonic irrigation is obviously important. Similarly, in mucous colitis, colonic irrigations are beneficial if performed correctly with respect to technic and frequency. Very often putrefied material is obtained from the upper colon in instances in which the bowel movements have revealed very little of an abnormal nature. Careful examination of material obtained by colonic irrigation may yield considerable important information regarding the degree and character of digestion.

In chronic bowel conditions in which other measures have been unsuccessful the utilization of colonic irrigation is sometimes gratifying. It is on this account that patients with mucous colitis, intestinal stasis (due to various causes) and so-called "intestinal toxemia" often finally are advised to employ this measure. However, it seems too much to expect that other chronic conditions should also respond satisfactorily to the same procedure and yet as already noted remarkable results have been reported in the treatment of anemias, rheumatoid conditions and various chronic low grade infections. If it accomplishes nothing more the irrigation removes most of the colon contents which, in turn, leaves the bowel empty and supposedly at rest.

Another use of colonic irrigation as an aid in diagnosis is its efficacy in clearing the colon of gas and hardened feces so that roentgen ray studies of the gallbladder, kidney or bony framework can be accomplished with greater accuracy. Clearing the bowel before a proctoscopic or sigmoidoscopic examination is likewise essential before a reliable study can be made, errors in diagnosis are not infrequently attributable to the omission of careful preliminary preparation.

When constipation is thought to be due to some obstructive lesion either intraluminal (neoplasm) or extraluminal (adhesions Jinks) a course of colonic irrigation may be very helpful in deciding upon the urgency or necessity of surgical intervention. We have had many patients under our care who have been spared operation owing entirely to the preliminary employment of irrigations resulting in bowel evacuations. If, on

the other hand, bowel movements do not occur, operation may seem more clearly indicated

It is evident, therefore that colonic irrigation is indicated in most conditions which interfere with the eliminative or absorptive properties of the large bowel, it may also be indicated in other colonic affections but always only as an accessory measure

Limitations—Since colonic irrigation is directed to the elimination of toxic products from the bowel its use must be limited by what is definitely known of the underlying cause of that condition The connection of intestinal toxemia with constipation is not at all clear for it has been demonstrated by many investigators that many of the most stubbornly constipated individuals present none of the evidences of so-called "intestinal toxemia" Moreover many individuals relieved of constipation still retain those symptoms which *in toto* have been termed by many as intestinal toxemia The unscientific and irrational conclusions advanced concerning irrigations have further limited their use In the first place, it is not as evident, as some would have us believe, that in patients with chronic constipation the bacterial content of the bowel is increased or modified Regarding the discharge of mucus, it has been demonstrated definitely that repeated irrigations are accountable in many instances for its production, that in other words, irritation of the mucous membrane has followed the procedure The authors have actually observed such changes in normal healthy dogs subjected to controlled experimental study While irrigations have been advised as a panacea for many ills the point to be stressed is the reaction in the opposite direction and thus arises a limitation which has often tended to swing to the other extreme, the condemnation of a therapeutic measure which may be of definite value when employed with proper limitations Furthermore, many of the modern systems of colonic irrigation are very complicated and this, too, limits their use

A procedure that has also been practiced is catheterization of the cecum This is limited in its use, however, for accord-

ing to Wiltsie it requires an unusually skilful operator to accomplish this intubation successfully in more than 50 per cent of attempts He attributes the failures to "spasticity, irritable or loaded colon, gas and sharp angulations" It would seem that such a procedure is entirely unnecessary in the light of our present knowledge, for we know that a large enema will reach the cecum in a very few minutes and this likewise occurs when barium is injected rectally, preliminary to roentgen ray studies

Treatment by colonic irrigation should always be preceded by roentgen ray studies to rule out the presence of obstruction and tumors as well as any other contraindications Hemorrhage from malignant disease has been produced by blind passage of the tube The introduction of the long tube is especially fraught with danger and in unskilful hands perforation has been known to result Not uncommonly unpleasant reactions follow colonic irrigation and although the method itself may be responsible another explanation has been offered, namely, that an incompetent ileocecal valve may allow a regurgitation of colonic contents into the ileum with absorption and consequent "toxic" symptoms Since modern research has demonstrated so much regarding the effect of vitamin deficiency on the gastro-intestinal tract it would seem that many of those colonic conditions in which irrigations are employed cannot possibly be benefited except temporarily since the basic disturbance is one of avitaminosis A well balanced diet is indispensable in the treatment of many of these conditions and deserves a trial period of treatment before measures such as colonic irrigations are employed except perhaps as temporary accessory aids Nevertheless, if the irrigation outfit consists of heavy or hardened rubber, its introduction is really dangerous to a diseased bowel tissue whether this affection is due to avitaminosis, ulceration or infection

Bastedo calls attention to the disadvantage of using frequent medicated irrigations of sodium bicarbonate solution as a solvent for colon mucus He states that "it does not dissolve the thick heavy masses of mucus found in mucous colitis, it unduly activates the kidneys, it may overalkalize the bowel and

the patient, and, not infrequently, it generates undue amounts of gas" He has had a "number of complaints of colic from sodium bicarbonate, while in the same patients plain water did not arouse colic" Plain water and normal saline are the simplest and most efficient irrigating fluids and since it has been shown that strong antiseptics are likely to irritate the bowel rather than to lessen the bacterial content their employment is limited with the exception of perhaps such preparations as gentian violet and other aniline dyes which have a specific action As a matter of fact continuous irrigation with water cleanses the bowel more thoroughly than can be expected from any antiseptic solution Nevertheless, excessive irrigation is contraindicated not only because it becomes irritating but also because bowel absorption and activity may be interfered with to the extent that nutritive material is lost and irregular bowel action produced In addition, it often consumes more or less of the patient's vitality, a factor too frequently overlooked Even when none of these contraindications exist the irrigation habit should not be encouraged for self-medication of any type is bound to produce harmful effects both physically and mentally

Nausea, cramps, epigastric pressure, abdominal distention, weakness and anal irritation are some of the symptoms which may be produced by colonic irrigation The degree of distress produced depends largely upon the experience of the operator Ordinarily there need be no symptoms if the irrigation is carefully administered but too much pressure, too much fluid, hurry, lack of gentleness or too stiff a tube will undoubtedly bring on untoward reactions It must, however, be borne in mind that certain individuals are hypersensitive to enemas and irrigations In such patients, symptoms of shock may be induced by the slightest attempt to apply these measures

Bastedo does not believe that colitis or permanent dilatation of the bowel can result from the use of colonic irrigations, though we are firmly convinced that permanent damage to the bowel may be brought about by their undue and unskilful employment

Friedenwald and Feldman have reported upon the effect of the prolonged use of colon enemas in animals, because it was their experience that the all too frequent use of enemas and irrigations led to the production of certain colonic affections, as well as nervous intestinal disorders In a well-controlled series of animal experiments they administered plain water, soap water, cotton seed oil, sodium carbonate solution, neutral acriflavine solution, camphor water, ammonium chloride solution, and dilute hydrochloric acid They conclude that enemas used over a long period of time led to more or less bowel disturbance, that even simple water enemas may produce mild inflammatory changes, that soapsuds enemas produce more marked inflammatory changes while oil enemas produce less irritation, that acriflavine (1 3000) and camphor water (U S P) cause but slight disturbance of the bowel and that irritating chemicals such as sodium carbonate, ammonium chloride, and hydrochloric acid, even in weak solutions, cause inflammatory changes ranging from mild processes to extensive ulcerations and necroses

In connection with the discussion of its limitations, the question arises again as to the inherent value of enemas and irrigations and in the consideration of this problem, the views of various observers are by no means in accord From the point of view of production of mucus Soper's experience leads him to the conclusion that the more one irrigates, the more mucus one gets He believes that lrrigations incite the secretion of mucus and if continued sufficiently long "foul smelling material" can be secured in persons with normal colons On the other hand, Bastedo finds that the slow, careful Introduction of from 6 to 10 gallons of water is a valuable, therapeutic procedure in the treatment of mucous colitis, intestinal putrefactive toxemia, as well as in cases in which a focus of infection is believed to reside in the bowel Many are convinced that the results of colonic irrigations are always only temporary, that they produce bowel injury and that during their use other valuable procedures are left unemployed Soper points out that it is not possible to wash the intestinal mucous membrane clean, be-

cause fecal contents must continue to enter the colon from the ileum

Colonic irrigations are contraindicated in severe cardiac disease hypertension, aneurysm, advanced arteriosclerosis, severe anemias with their associated weakness, high fevers, exophthalmic goiter, highly nervous states, acute intestinal ulcerations, perforation, hemorrhage, old age and other conditions resulting in debility or lack of resistance They should not be employed in individuals hypersensitive to the procedure itself In conditions such as anal stricture colonic irrigations are obviously contraindicated In severe hemorrhoidal conditions as well as in acute pruritus ani or anal eczema the procedure should be omitted Moreover any acute ulcerative condition of the colon, rectum or anus is sufficient contraindication in the majority of cases In such disturbances there is always danger of perforation or hemorrhage In any chronic disease which has taken its toll of the patient's vitality colonic irrigations, if employed at all, must be administered with the greatest of care and caution

The treatment may produce local injuries such as abrasions, irritations, hemorrhoids or stretching The general symptoms of debility, nausea, pains, vomiting, cold sweats have already been mentioned Sometimes, due to the use of an unsuitable or improper dosage of a drug, toxic symptoms may follow, but this should be rare The criticism that colonic irrigation leads to habit formation has already been referred to and we are thoroughly convinced that there are definite instances of habit formation which lead not only to disturbance of the bowel but of the nervous system as well

Technic—In considering technic it is wise to caution against casting aside the simple single or double tube irrigating arrangements for the more elaborate apparatus As already noted there is no object in having the colonic catheter more than 2 to 3 inches in length, especially since it can be demonstrated that fluid injected into the rectum generally reaches the cecum in less than ten minutes In the light of such information it

seems irrational to attempt to introduce catheters into the cecum

Attention has been directed to the many devices for applying colonic irrigation and it is now known that catheters with separate inlet and outlet tubes are not always satisfactory According to Russell the best of the other systems can be divided roughly into two groups (1) Those in which the irrigating fluid enters and leaves the bowel by the same channel, the withdrawal of the fluid being effected by siphonage and controlled by the person administering the treatment and without any intervention on the part of the patient, (2) those in which the catheter is only provided with an inlet channel, the expulsion of the irrigating fluid and bowel contents taking place around and through the catheter which, however, remains in position during the treatment and is not dislodged when defecation occurs The treatment as far as the patient is concerned, is entirely passive in the first group while in the second, the patient himself expels the irrigating fluid from the bowel The passive reaction in the first method does not induce active contractions of the bowel musculature, whereas in the second method the patient actively contracts the voluntary muscles concerned in defecation and thus induces contraction of the colonic muscles In our experience both methods are equally satisfactory though in weakened and debilitated individuals the passive method is found less strenuous The liquid utilized in a colonic irrigation should usually be about body temperature although many have found 104° F more satisfactory It is important that the fluid be allowed to flow in slowly so that defecation reflexes are not excited inasmuch as the primary object of a colonic irrigation is to reach beyond the defecation area According to Bastedo and many others liquid from a tube inserted only 2 or 3 inches will pass to the cecum in two to three minutes It has also been repeatedly demonstrated by roentgen ray examination that in almost every instance a tube inserted beyond 6 inches merely coils upon itself in the rectal ampulla, on the basis of such data the distinction between low and high irrigations seems unwarranted The simplest types of fluid used

are plain water, saline and soda In our experience in properly selected cases, the following technic of colonic irrigation has been found very satisfactory The colon is irrigated with a solution containing 2 drachms of sodium bicarbonate and 1 drachm of table salt to each 2 quarts of warm water using the return flow, Y or T glass irrigator The patient is placed on the right side, the rectal tube inserted about 1 inch and 4 ounces of the solution is allowed to flow in slowly and permitted to drain until a quart has been utilized This overcomes the sensitiveness of the rectum The tube is now inserted for a distance of 4 to 6 inches and 1 pint of the solution is allowed to flow in and again drain, the procedure being repeated until about 15 quarts are consumed The patient is then turned on the left side and the same procedure continued until the return flow appears quite clear About 5 quarts of solution are utilized with the patient upon his back Prior to the treatment in some instances, about 4 turpentine stupes are applied upon the abdomen followed by deep massage During the irrigation a warm stupe is allowed to remain on the abdomen Before the patient is turned upon his back another deep massage is given If any infection of the bowels or rectum is discovered the following enema is given before the irrigation

Olive oil, 8 ounces
Soapsuds, about cupful } Mix with 2 quarts of warm water
Salt, teaspoonful

According to Bastedo 5 to 9 gallons of plain water are best utilized for an irrigation, with the patient on his left side for the first gallon and on his back for the remainder The reservoir bag is hung low so as to give about 1½ feet of pressure and the water allowed to run in very slowly, taking about an hour Objection has been raised by many to the use of soapsuds as an irrigating fluid because it is unsatisfactory and irritating Russell finds a hypotonic solution of sodium chloride one of the best fluids for routine use, 2 ounces to 8 gallons are advised When an antiseptic action is desired his choice is made from albargin, dimol, hydrogen peroxide, ichthyol, monsol,

potassium permanganate and silver nitrate Emetine is one of those employed in cases of dysentery, tincture of belladonna in spastic conditions of the bowel, strychnine for its tonic effect and some form of opium for sedation and relief of pain In our opinion an infusion of chamomile tea is useful in spastic states Acriviolet in a concentration of 1 35,000 has been recommended for its highly germicidal properties It is said to be much more effectual than acriflavine However, acriflavine is a very satisfactory medicinal agent. Mercurochrome has also been recommended and used When astringents are required Russell finds alum, copper sulphate, iron chloride, lead acetate or tannic acid useful, for its absorbent cotton he advises kaolin and in parasitic infections, male fern, pomegranate bark, quassia, santonin and turpentine are employed Others have laid great stress on the implantation of acidophilus cultures in the cecum and various parts of the colon, but in general this seems an ineffective plan of therapy In our opinion many of the medicinal preparations mentioned above are to be avoided in favor of other forms of therapy

It is important, however, to call attention to the following practical points in technic Of the special lavage apparatus the horizontal douche introduced by De Langenhagen at Plombières is perhaps one of the most widely employed There is little to be gained by even calling attention to all of the more complicated instruments such as the Studa chair, the gymnacolon apparatus, the subaqueous intestinal bath apparatus, the Honsaker colonic lavage apparatus, the Springfield infirmary apparatus and others Catheters may be prepared for single injection or continuous irrigation even with the simple tube methods It matters very little whether the patient is on his right or left side or back, but in general it is desirable to change from one position to the other The temperature of the solution may vary within a wide range (45° to 122° F) but the most satisfactory routine temperature is 104° F although solutions of higher temperature are recommended in some cases of spastic constipation and colic and colder in atonic constipation The amount of fluid used also varies greatly but the

decision as to quantity depends upon the nature of the affection and upon the capacity of the patient, usually 1 to 2 pints at a time are adequate The pressure under which the solution is applied varies with the type of apparatus but it is always desirable to allow the solution to flow in slowly by gravity Usually the fluid should be retained less than five minutes and at least 2 (usually more) injections should be given The catheter should always be suitably lubricated and the irrigation best given early in the morning before breakfast or about three hours following the evening meal

Summary—In summarizing in a general way it is our opinion that if colonic irrigations are correctly used in selected cases they fulfil an important therapeutic need The conditions in which they are probably most helpful are mucous colitis and intestinal stasis but there are a number of other dysfunctions in which their occasional use is indicated The simpler the irrigating fluid the better and it is generally conceded that plain water, salt solution and bicarbonate of soda, properly diluted, are most desirable except in those instances in which some specific medicinal agent is indicated We are inclined to favor the use of the ordinary soft rubber rectal tubes However, any simple apparatus which would facilitate the procedure is acceptable if at the same time it is effective and safe Many of the more complicated apparatus which have been advertised are not to be recommended The fact that a simple apparatus is so satisfactory is one of the greatest objections to the more complicated ones Medical supervision is essential in all cases in which colonic irrigation is advised and the proper interval between treatments must be specifically directed The public and nonprofessional physical therapists should understand this necessity in view of some of the contraindications to colonic irrigation Some of these dangers are mechanical trauma to mucous membrane causing hemorrhage, possible perforation, overdistention of the bowel with loss of tone and rectal sphincter damage

BIBLIOGRAPHY

Bastedo W A. Colon Irrigation New England Jour Med., 199 865 1928
Bastedo W A. Colon Irrigation Jour Amer Med Assoc., 98 734 1932
Friedenwald J., and Feldman M Experimental Studies on the Effect of Prolonged Use of Colon Enemas Upon the Bowel in Animals, Amer Jour Surg., 11 23 1931
Friedenwald J., and Morrison T H The Modern Treatment of Digestive Diseases International Clinics 1 133 1932
Friedenwald J., and Morrison S The Significance of Membranes in the Mucous Form of Colitis, Jour Lab and Clin. Med., 18 1242, 1933
Montague J F History and Appraisal of the Enema Medical Record 139 91 1934
Russell W K Colonic Irrigation William Wood & Co., Baltimore 1932
Russell W K Colonic Lavage Fallacies and Facts Brit Jour Phys Med., 8 24 1933
Soper H W Colon Irrigations Jour Amer Med Assoc., 98 1677 1932
Wiltsie J W Colonic Therapy Theory and Practice Arch Phys Therapy x Ray and Radium 14 479 1933

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR THEODORE H MORRISON

FROM THE GASTRO-ENTEROLOGICAL CLINIC OF THE DEPARTMENT OF MEDICINE UNIVERSITY OF MARYLAND

IDIOPATHIC ULCERATIVE COLITIS WITH A REPORT OF AN UNUSUAL CASE

IDIOPATHIC ulcerative colitis is of sufficient importance to have interested numerous workers, not only gastro enterologists and proctologists, but also bacteriologists and surgeons as well, so that a voluminous literature has been accumulated This, no doubt, has been considerably augmented by the bacterial etiologic controversy Since this disease is apparently increasing in prevalence and since it presents many difficult problems it remains of widespread interest The purpose of this paper is to summarize our knowledge of this subject and to report an interesting case with an unusual surgical attack

Chronic ulcerative colitis is known by a host of other names, some of which are nonspecific ulcerative colitis, colitis ulcerosa, suppurative colitis, primary, hemorrhagic and colitis gravis It was first described by Wilks in 1875 Credit for much of our knowledge of this subject is due to White who in 1888 reported eight cases and fully described its pathologic and clinical picture Gemmel in 1898 called attention to the fact that this condition was different from dysenteric colitis which occurred in the course of other diseases Idiopathic ulcerative colitis, which occurs sporadically, was definitely established as distinct from that form of bloody dysenteries which occur in epidemics by the investigation of Ivre, Vedder and Duvall who showed the cause of the latter to be due to infection with B dysenteria Shiga

Etiology.—There has been a great difference of opinion as to the etiology of this disease Various types of organisms have been considered as having causal significance but none as yet has been generally accepted as of specific importance Such observers as Leusden, Thorlakson, Kuttner, Rosenheim, Zweig, Hurst, Saundby and Hawkins consider the dysentery bacillus as the original invader

Nabarro isolated B dysenteriae from a case of ulcerative colitis in 1912 Young recovered Flexner bacilli from one case and Dudgeon from two cases Winkelstein obtained members of the Flexner or Shiga groups from four cases Mackie after a thorough bacteriological study undertaken to obtain additional evidence concerning a fundamental relationship between the two diseases found that in a series of 83 unselected consecutive cases of chronic ulcerative colitis in New York City there was present cultural or serological evidence of bacillary dysentery in 42 per cent Mackie believes that B dysenteriae may play a much more important rôle in the production of chronic ulcerative colitis than is usually recognized He also states that at the present time it is impossible to evaluate exactly the importance of these and other organisms which have been advanced as etiologic factors in this disease Whether or not some cases originate as a form of bacillary dysentery is still problematical since these organisms are difficult to find in the chronic cases and the agglutination reaction is likewise negative except in the early acute cases and besides it is not entirely dependable as a means of diagnosis The consensus of opinion in this country, however, is against the theory that ulcerative colitis is a modified form of bacillary dysentery

Torrey in a review of the bacteriological findings in his series of 28 cases of nonspecific ulcerative colitis isolated a strain of Bacillus coli in 25 Virulent strains of B coli have been considered by a number of investigators of prime importance as a cause of this disease Satterlee and Bassler subscribe to this idea Torrey states that there is no convincing experimental evidence for this view Rolleston and Mummery have considered the pneumococcus as a possible offender Torrey says he has never

encountered it in hundreds of examinations of fecal material and he doubts whether it can thrive in the human colon or infect its walls Among the more uncommon intestinal bacterial types which have been noted from time to time as occurring in the colon of these cases are B pyocyaneus, B proteus, and B mucosus capsulatus

In 1924 Bargen published his work on the etiology of ulcerative colitis As the result of extensive experimental investigations and the constant finding of a Gram-positive, lancet-shaped diplococcus possessing special cultural characteristics, he concluded that this organism must be the specific cause of the disease The evidence on which Bargen bases his concept is the constancy of the finding of these organisms, the similarity of the strains from different cases, the experimental production of lesions in animals and the beneficial effects obtained in patients by use of vaccines and sera derived from them In their most recent article Bargen and Buie summarize their bacteriological opinion by stating that after a decade of study they still believe that chronic ulcerative colitis is a specific disease entity in which the Bargen organism "plays a part in the causation of most cases" This claim, has not, however, been confirmed by others Paulson in an exhaustive bacteriological study seems definitely to have refuted Bargen's work

Some of the other factors mentioned that may be of etiologic significance in this disease are metabolic, bacteriophagic, allergic vagotonic, psychogenic, enzymatic, focal infection and avitaminosis On a vagotonic basis, Brown and Mallory have seen patients with spastic constipation and mucous colitis finally develop chronic ulcerative colitis

On a similar basis the "trophic neurosis" theory is emphasized by Nelsen who states that this disease in its general manifestations suggests some disturbance in the nervous mechanism of the bowel wall with secondary changes in the protective forces in the mucosa In this connection, he calls attention to his observation in some cases of a very definite hypertrophy of the meissnerian (submucous) and Auerbach (myenteric) plexuses

As a result of a recent analysis of a series of 75 cases Mackie

concludes that the available evidence does not support the unitary theory of bacteriological primary invaders The findings in his group point to a rather more complex mechanism including primary and secondary infection, deficiency states resulting from inadequate diet or to small intestine involvement, and an allergic state to certain foods and races of bacteria

It is quite possible that an individual susceptibility may exist and as a result of a temporary lowering of resistance from an upper respiratory infection, emotional strain or overwork, plus some combination of these factors may bring about this disease It has, however, been known to occur as an acute invasion in individuals in apparently perfect health

As a result of this summary, it is apparent that the etiology of this most interesting condition is still in doubt and consequently it should be considered in the light of a syndrome and not as an entity

Incidence—This disease does not occur in epidemics It is most commonly seen in the third, fourth and fifth decades of life although it can occur at any age period Our youngest patient was thirteen and our oldest sixty It has been reported in children of seven and in adults over seventy There does not seem to be any particular difference as to sex, males and females being about equally affected The disease may be found anywhere in any season

Pathology—The first recognition of this disease as a pathologic entity occurred in 1885 when Sir William Allchin before the London Pathological Society exhibited a specimen illustrating the lesions of chronic ulcerative colitis Since that time numerous contributions have been made which have added much to our knowledge of the pathology of this condition The publications of Hale White, Smith, Lynch and Felson, Crohn and Rosenberg, Buie and Bargen, and Brust and Bargen, are especially noteworthy The process usually begins in the lower bowel in the form of a diffuse inflammatory reaction involving the wall of the colon The disease may involve the whole or some of the segments of the large intestine In the milder cases only the rectum and sigmoid or both may be affected, whereas

in the more severe ones the entire colon and even a small stretch of the terminal ileum may be the seat of the disease The mucosa in the early stages shows an intense injection due to the marked hyperemia and edema that is present The submucosa and muscularis are infiltrated with small round cells The surface bleeds on the slightest trauma There is a diffuse exudate of mucopurulent material which is spread over the bowel surface Small superficial erosions varying in size from a pin-point to several millimeters in diameter are seen all along the involved areas As the condition progresses the ulceration may involve the submucosa and muscularis and occasionally intramural abscesses may form Only in the very severe cases and then only rarely does the lesion spread to the serosa producing single or multiple perforations with accompanying peritonitis Finally, as a result of long-continued inflammation with remissions and exacerbations the bowel may become anchored and rigid due to thickening and fibrosis of the entire bowel wall The mucosa may be largely destroyed by confluent ulcerations leaving only islands of fairly normal tissue A polypoid condition may develop in these islands and such areas may occasionally undergo carcinomatous changes Virchow, many years ago, called attention to the lesions that he designated as "colitis polyposis cystica' which results from a blockage of the gland ducts by scar tissue with consequent retention of secretion in the crypts

Buie described the sigmoidoscopic picture in the following stages (1) A diffuse hyperemia (2) edema throughout the involved area associated with thickening and friability of the mucous membrane (3) miliary abscesses present themselves under the mucous membrane, and (4) rupture of the abscesses leaving miliary ulcers These are the four chief periods or stages of activity The period of quiescence is one of gradual recession and with it the active pathologic process subsides The inflammatory changes disappear either partly or entirely The ulcers heal and characteristic pocklike scars remain As a result of exacerbation another type of ulcer is superimposed on the small petechial ulcer due to secondary infection

Brust and Barker state that it is difficult to tell how a given

case of chronic ulcerative colitis will act "The colon may heal or as a result of intense destruction exhibit scars, strictures, mucosal ridges or tags of mucosa The mucosal tufts may at any time begin to give evidence of true adenomatous hyperplasia and may eventuate in multiple adenomas studding the colon And lastly, but fortunately rarely, carcinoma may supervene as an early or late complication"

Symptomatology—The disease presents two main types, one characterized by an acute fulminating illness, and the other by a rather chronic course with a more insidious onset In the former, the onset is very abrupt with abdominal distress, many bloody, purulent discharges, tenesmus, and prostration This form progresses rather rapidly with the development of marked emaciation, leukocytosis, hyperpyrexia of a septic type and severe secondary anemia Chills, sweats, nausea and vomiting are additional symptoms presented by this group indicating the presence of an intense toxemia In the other form, the symptoms come on more gradually consisting of flatulence, weakness, abdominal discomfort and the passage of loose stools streaked with blood and mucus These patients may lose a little weight and become somewhat anemic, but, as a rule, they are not aware of any marked departure from health Which course the disease will take will depend on the extent of the involvement of the large intestine, the rapidity of the development of the disease, and the resistance of the patient In the milder types, some may, after a few weeks or months of a moderate diarrhea, recover and be permanently well Acute exacerbations in this group are relatively rare and when they do occur are not severe In the severe type the disease may run a stormy course from the onset with intractable diarrhea great prostration, toxemia, rapid loss of weight and general failure The majority, however, strike a middle course and with exacerbations and remissions may go on for years before the final stages are reached During the active stages of the disease a moderate leukocytosis is present In practically all a secondary anemia is the rule, and in the very severe advanced cases the hemoglobin may go as low as 20 per cent

Diagnosis —In order to accomplish the best results an early diagnosis is very important The history in the majority of cases is very helpful, yet in some, especially in the early stages, when the disease is still limited to the rectum, stasis may be present. The usual history obtained is one of a disease chronic in character with remissions and exacerbations Any chronic or subacute diarrhea with the passage of blood, mucus and pus in the stools should suggest the diagnosis of chronic ulcerative colitis if amebas and dysentery bacilli are not found The sigmoidoscopical examination should be relied on principally in making the diagnosis of this condition It should be performed in every case and as early as possible The typical lesions as described under Pathology can be visualized by the sigmoidoscope Familiarity with and careful study of the picture together with examinations of the stool and scrapings will help to rule out any of the specific diarrheas such as those due to tuberculosis, lues, cancer, amebic and bacillary dysentery

Roentgenological studies are useful not only in the diagnosis of chronic ulcerative colitis but also by repeated barium enemata the response to treatment can be traced The findings will depend on the extent and the degree of involvement of the colon If the lesion is early the films may show nothing abnormal Only after the disease is well advanced can the characteristic picture be demonstrated By the barium meal hypermotility of the entire gastro-intestinal may be noted It is only by means of the barium enema, however, that the typical picture is revealed The thickened bowel wall is indicated by a narrowing of the lumen and an absence or diminution of the haustrations Areas of a fuzzy outline or of irregular defects may be seen indicating the sloughing and ulcerating lesions In the late stages areas of contraction throughout the colon resembling a string of sausages is typical of this condition Since the normal haustration of the bowel disappears in the affected part, it is possible to determine the extent of the disease by roentgen examinations When recovery takes place the haustration returns except in the very chronic cases According to Hurst the proximal part of the colon is the last to be involved and the

first to recover, the disease almost always begins and ends in the rectum and pelvic colon, so that sigmoidoscopy detects the earliest stage of the disease, and when the mucous membrane of the rectum and pelvic colon are found to be no longer inflamed it may be assumed that the same is true of the whole colon

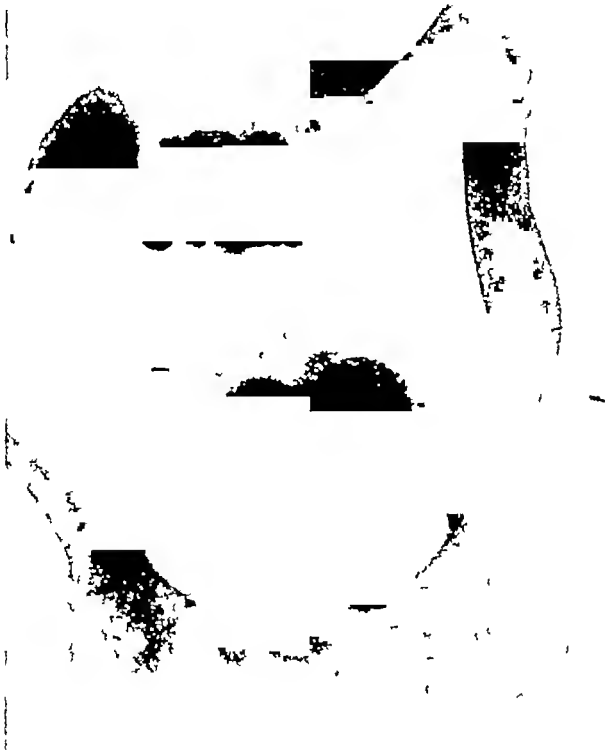


Fig 173 —Colon enema illustrating rigidity of left colon with loss of haustration

Polypoid changes are best demonstrated by the double contrast enema, air being injected cautiously into a bowel thinly coated with barium Carcinoma, lues, tuberculosis and extreme atony can be differentiated roentgenologically from ulcerative colitis

Mackie reports that x-ray examination of the small intestine

in his series of cases has revealed two forms of abnormality previously unrecognized A disturbance of the motor function characterized by delay in the progress of the opaque meal with dilatation of certain segments, and structural changes in the wall suggestive of acute exudative inflammation

Fig 174 —Roentgenogram showing marked irritability with rapid emptying of colon following evacuation of barium enema

Treatment—The earlier the diagnosis is made and the sooner suitable therapeutic measures are instituted the better the prognosis The milder cases in which the disease is limited to the rectum and sigmoid may recover spontaneously or with very little treatment whereas the severe fulminating types may

remain refractory to any mode of attack The specific treatment of this disease awaits the determination of its specific cause or causes Even at the present time there is every reason to be hopeful as to the outcome of many of these cases A minimum follow-up period of three years is a prerequisite for claiming cure, some patients have been known to experience recurrences after five years There is no doubt that the results of treatment in the severe chronic cases with its tendency to acute exacerbations are very disappointing, yet we have even seen some of these recover and remain well

The treatment should be very comprehensive There is great need for encouragement, physical, mental and physiologic rest Rest in bed with plenty of fresh air and sunshine is of the utmost importance Focal infections should be eradicated The diet, except in the very acute stages, should be rather liberal, high in calories and rich in vitamins and minerals and low in roughage Such a diet would include plenty of butter, milk, eggs, fruit juices, tomato juice, puréed greens, tender red meat and liver Cod liver oil may be added The only drugs indicated in this disease are those that will allay intestinal peristalsis and check the diarrhea, such as bismuth, kaolin, paregoric and other opiates when necessary Calcium and parathormone administration has been advocated by Haskell and Canterow

Colonic irrigations are as a rule harmful, producing anal irritation and an increase in the rectal discharges However, in some cases, these make the patient feel more comfortable by removing fecal matter and gas Some of the many medicaments that have been used for irrigation purposes are tannic acid, acriflavine, mercurochrome, gentian violet, argyrol, silver nitrate, and potassium permanganate These are especially helpful when there are anal and rectal ulcerations In these cases Soper finds the topical application of some antiseptic medicament or of some soothing powder such as equal parts of calomel and bismuth subcarbonate gives much relief Felsen advocates the continued use over prolonged periods of intestinal oxygenation

Bargen depends mainly on the use of his concentrated serum

which is injected intramuscularly in gradually increasing doses Later on he uses a vaccine preferably prepared from the patient's own lesions He, of course, advocates the usual supportive measures in addition to his sera and vaccines His results with an extensive clinical material are very remarkable. Since no specific organism has as yet been definitely established as the cause of this disease, the beneficial effects obtained by the use of vaccines and sera may perhaps be explained on the basis of any foreign protein therapeutic reaction Hurst, Crohn and others have obtained wonderful results with the use of polyvalent antidysenteric sera Brown and Paulson cite a startling effect obtained by the intramuscular injections of mixed anti pneumococcus serum It seems to us that in stubborn cases we are justified in trying any of these measures

Mercurochrome intravenously has been advocated by Young, Bassler and Andresen We are opposed to any form of intravenous therapy with substances which may prove irritating and toxic Transfusions on the other hand, of 250 to 300 cc of blood repeated at intervals of four or five days as necessary are very valuable in supporting the patient with a severe anemia Glucose, administered intravenously in the acute stages or when food is poorly tolerated, is also helpful

The question of surgical intervention is always difficult to decide There are those who claim that surgery is never indicated except perhaps for the relief of complications such as stricture or abscess formation Berg, on the other hand, suggests early radical resection of the involved portion of the bowel We feel that conservative surgery, preferably ileostomy, since it puts the colon completely at rest, should be considered not too late in the course of the disease and a decision should be reached only after a thorough medical and surgical consultation Colectomy is a dangerous operation and is rarely employed Colectomy, after ileostomy, is an operation of value because it can be performed in two stages without prohibitive risk The continuity of the bowel after ileostomy should not be restored until normal mucosa is seen sigmoidoscopically and there is definite evidence that the lesion in the colon has healed

At this point, in view of the case report to be presented, it might be appropriate to quote Rankin's ideas on the treatment of multiple polyps of the colon "Surgical extirpation of the entire large bowel is a formidable procedure and should not be undertaken lightly The extirpation of the colon for diffuse lesions may be undertaken with two objectives in mind If the adenomata are largely confined to the colon proper, and there are only a few scattered tumors in the rectum, one considers sacrifice of the large bowel and the transplantation of the ileum into the rectum, thus saving the sphincteric mechanism Where the rectum is involved in such a way as to preclude saving it, a three-stage procedure is most desirable This procedure consists of first, ileostomy, second, subtotal colectomy down to or near the rectosigmoid juncture, and third, a combined abdominoperineal resection of the rectosigmoid and rectum These three stages evolve a rather prolonged procedure, but I believe increase the safety of the maneuver A single-barrel ileostomy is established in the right lower quadrant through a McBurney type of incision Once this ileostomy is adequately working, and the loss of fluids from it has been compensated for and at the same time the terminal ileum has taken on some of the function of the large bowel, and the fecal current becomes semisolid, one may consider the second stage I believe it is perfectly feasible to wait weeks, and even months, between the first and second stage if it is not felt that malignancy has already developed The rapid loss of body fluids following the establishment of the ileostomy necessitates a considerable amount of rehabilitation before the individual is able to stand an extirpation of the colon without grave danger The second stage consists in the removal of the colon down to or near to the rectosigmoid juncture This is accomplished through a long left rectus incision Again a period of time is allowed to elapse between the subtotal colectomy and the combined abdominoperineal resection of the rectum "

The following case report will illustrate some of the points considered in this review and it also presents an unusual surgical approach The patient was a white, single woman, aged

twenty six years who first consulted us on July 10, 1932, at that time she gave a history of persistent diarrhea for over one and a half years Except for having had measles, mumps and whooping cough as a child, her past history was quite negative She was subject to head colds and after one attack she developed "running ears" There had been no operations except tonsillectomy in childhood She was always inclined to be overweight and before the onset of the present illness she weighed 165 pounds In an effort to lose weight she had for some months been using drastic cathartics In September of 1931 she had been in a serious automobile accident, she was badly shaken up and her abdomen particularly was jarred The diarrhea which she attributed at first to the use of cathartics started insidiously but kept up even after the laxatives were discontinued and then gradually became worse following the accident The stools which at first were few in number, watery, containing much mucus, soon became more frequent and as many as 20 discharges occurred in a day The character also changed so that blood, pus and mucus were evacuated with every stool She lost considerable weight and when first seen by us she weighed only 106 pounds

At the onset of her illness she had several intervals when she seemed to be improving but in the six months preceding the present interview the condition has become much more severe, so much so that sloughs have recently begun to appear in the stools in addition to the pus and blood For the past three months she has been confined to her bed She had consulted several physicians elsewhere and the diagnosis of chronic ulcerative colitis was made The so-called Bargen diplostreptococcus was found in almost pure culture in her stools and an autogenous vaccine was prepared This was administered every other day over a period of a month starting with $^1/_{10}$ cc and increasing gradually to 1 cc Fifty cc. of a stock serum made by Mulford according to Bargen's directions were given intramuscularly over a period of five days but the only reaction was severe serum sickness There was no improvement whatever in the general condition In addition to the diarrhea

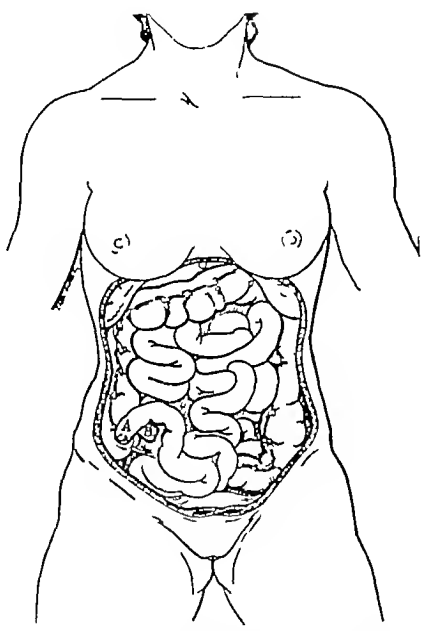


Fig 175 —Diagrammatic presentation of the first stage of the operation "A" denotes the ileostomy and "B" the ileal stump

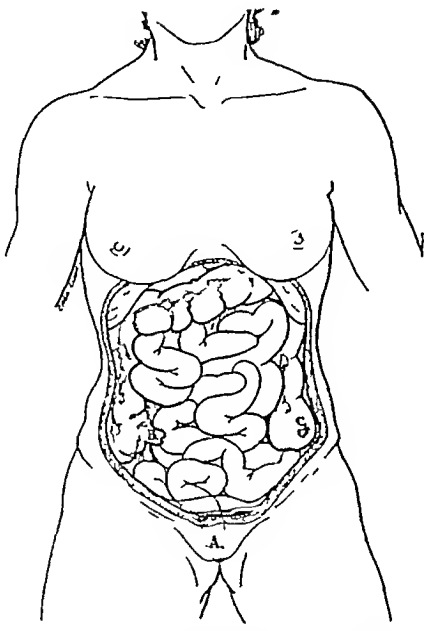


Fig 176 —Second stage with appendectomy (removed in first stage), "C" denotes the colostomy, the rectum and sigmoid resected and "A" represents the terminal ileostomy into the anal region

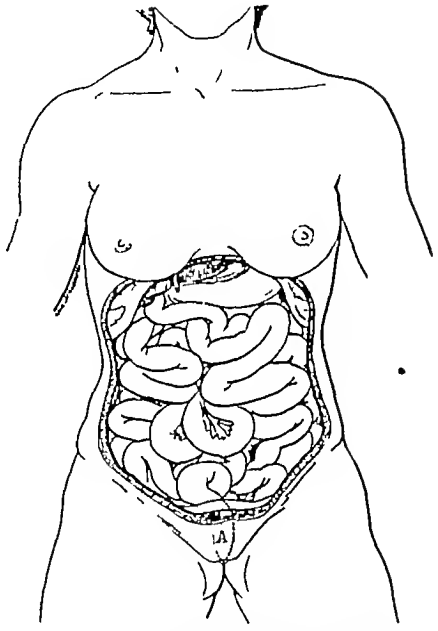


Fig 177 —Final stage—resection of remainder of the colon, including ileal stump

which now averaged about ten passages a day she complained of severe headaches, weakness, migratory joint pains, palpitation and dizziness

In December, 1931, she developed some hemorrhoids together with a small fissure In April of 1932 an ischiorectal abscess formed which was incised and drained Following this a fistulous tract developed

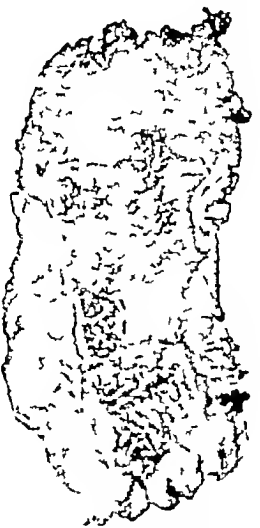


Fig 178.—Resected rectum with polyposis

The patient was sent to the hospital under our care for study and treatment on July 10, 1932 Her general appearance at this time was that of an undernourished, dehydrated individual who definitely gave the impression of being very sick She had lost considerable weight The eyes were prominent and protruded giving the appearance of a hyperthyroid state The

lungs were clear throughout, and the heart sounds were normal but rather rapid The abdomen was of the scaphoid type, very tender throughout but particularly so in the lower half The liver was enlarged 3 cm below the costal margin, it was smooth and not tender The tip of the spleen was just palpable The blood pressure was 118/74 The skin was dry and parched

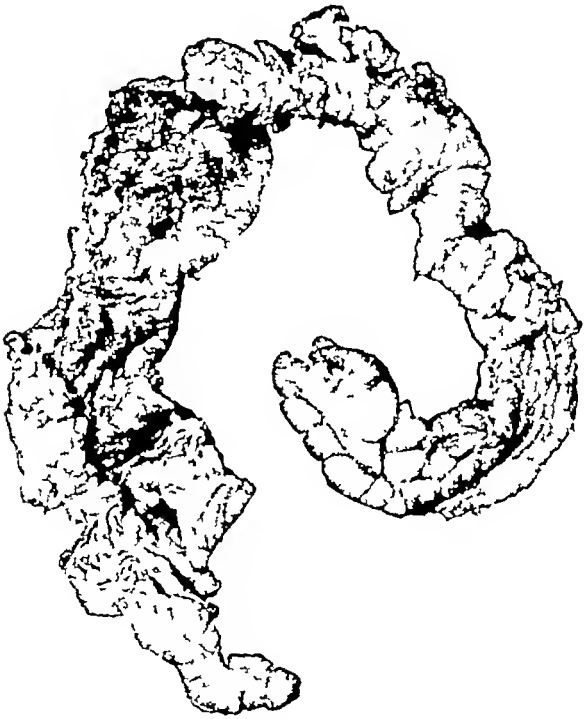


Fig 179—Resected colon with scattered areas of polypi

The temperature was elevated and later proved to be of the septic type Examinations of the stools have been persistently negative for the dysentery group and no amebae were ever discovered Pus, blood and mucus were always present in the stools A basal metabolic rate was determined to be minus one A fractional gastric analysis following an alcohol test meal showed no free hydrochloric acid over a period of one and a

half hours with a total acidity varying from four to twelve degrees The blood count on July 11, 1932, showed a marked secondary anemia, erythrocytes being 2,700,000 and leukocytes 11,200 with a normal differential count The value for the hemoglobin was 42 per cent Roentgen examination revealed a spastic, irritable gastro-intestinal tract with changes suggestive of chronic ulcerative colitis of the entire colon Sigmoidoscopical examination showed the typical picture of ulcerative

Fig 150—Photomicrograph showing polypi of colon

colitis and also a small rectal abscess and a fistulous tract The blood cultures were negative The Wassermann and Kahn tests were negative The urine was normal

As the result of these examinations we were certain that we were dealing with a rather severe case of nonspecific ulcerative colitis The treatment consisted of rest, transfusions, high caloric nonresidue diet, calcium lactate and parathyroid extract

Since the patient's progress was not at all satisfactory, surgical intervention was deemed advisable and on July 27, 1932, Dr Harvey B Stone performed an ileostomy, appendectomy, and excision of the rectal fistula After a rather stormy, early convalescence, she responded in a very satisfactory manner to transfusions and to other general supportive measures, so that on August 17, 1932, she was able to leave the hospital in excellent condition to continue treatment at home She

Fig 181 —Section showing the dilated glands of the mucosa of colon

weighed at this time 108½ pounds and her blood examination showed 4,000,000 red cells and 80 per cent hemoglobin She made satisfactory progress at home and returned periodically for examination

In October, 1932, when she first returned, she had gained 30 pounds, weighing 138, and her bowels were moving only twice daily through the ileostomy opening The proctoscopic examination revealed a hyperemic mucous membrane and a few

superficial ulcers The blood examination showed a total red count of 3,750,000 with a hemoglobin of 75 per cent.

On her next visit in January of 1933, she was doing very well, her weight being 134 pounds The blood examination was very satisfactory, red cells being 3,800,000, hemoglobin 72 per cent, and the proctoscopical examination showed considerable improvement but there were still some superficial ulcerations with

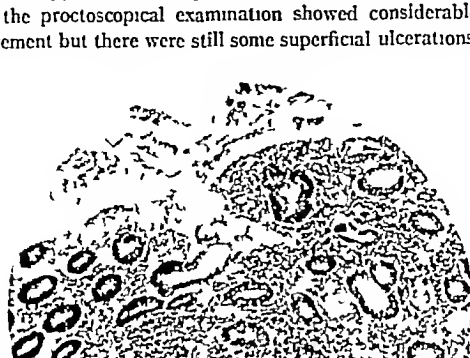


Fig 187.—Section showing inflammatory exudate in colon

some mucopurulent exudate The fistulous area had completely healed leaving only a minor scar

In May of 1933, she returned again when her condition was still very satisfactory She had one spell of diarrhea, brought on by worry over an illness of her father, but it was of brief duration At this time her weight was 132 The blood count showed a hemoglobin of 52 per cent and a red count of 2,700,000 As far as could be visualized through the procto-scope the appearance of the bowel was much better and there were no actual

ulcerations but some scarring and some mucopurulent material were observed At this time it was thought advisable to keep the ileostomy open for six months longer

In October, 1933, she reported a spell of bloody diarrhea following a "grippe" infection She was quite depressed over her condition for a while Her weight, however, remained satisfactory, 132 pounds Her blood still showed the marked secondary anemia, hemoglobin 56 per cent and the red blood

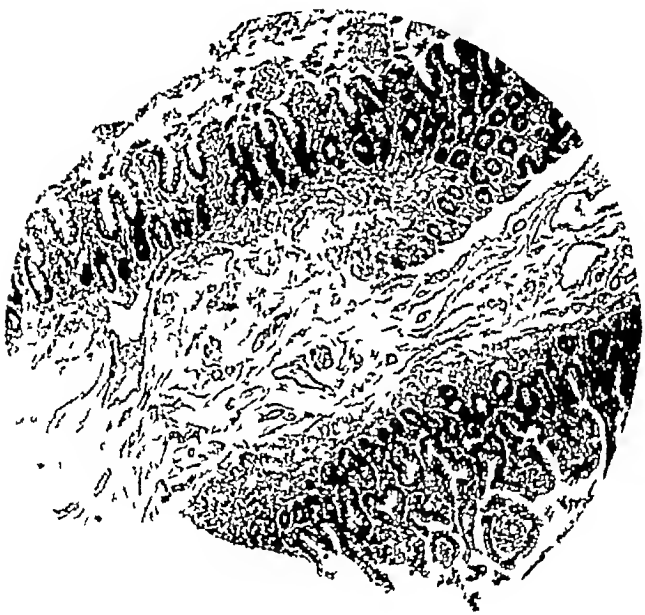


Fig 183—Section of terminal ileum showing ileitis

count 3,100,000 Moreover, the sigmoidoscopical examination revealed polyposis of the rectum and sigmoid Colectomy was considered advisable in view of this complication but the patient was doing quite well and it was finally decided to postpone this radical procedure for a short time

In January, 1934, the patient returned, complaining of having been greatly disturbed and embarrassed by uncontrollable bloody discharges from the anus This seemed to have been

aggravated by another grippal infection and the extraction of an infected wisdom tooth She had lost about 10 pounds in weight, was very nervous, restless and complained of having had to spend two to three hours at night passing these discharges until she became exhausted and was unable to sleep afterward The blood examination at this time showed a hemoglobin of 62 per cent and a red blood count of 3,500,000 with a white count of 10,200 The proctoscopical appearance showed the polypoid condition to be about the same as it was in the previous examination

Principally on account of the danger of malignant transition of the polypi and also because the patient was very unhappy and unwilling to go on with the ileostomy cup life, it was thought advisable to undertake the radical operation of colectomy

Since the rectum was involved and in order to do away with the ileostomy Dr Harvey B Stone decided to attempt total colectomy with the transplantation of the terminal ileum into the anal region with the hope of establishing some sphincteric control by plastic methods She was readmitted to the hospital on January 26, 1934, and after due preparation including transfusions the first stage of this plan was done on January 30, 1934 The operation consisted of resection of the rectum and sigmoid terminal colostomy, and terminal ileostomy through the rectal sphincter The technic of this stage was as follows

After routine preparation of the skin, a purse string suture was laid about the ileostomy stoma in the right lower quadrant Then following routine preparation of the abdomen with iodine and alcohol a low midline incision was made The abdomen was found to be fairly free from adhesions The sigmoid-colon was identified and the mesocolon incised on either side from the bowel edge to the base of the mesocolon The superior hemorrhoidal branch of the inferior mesenteric artery was identified with its accompanying veins and clamped divided and tied Peritoneal incision was then carried forward and downward around the anterior reflection of the sigmoid Sigmoid was then crushed and tied off with braided silk at the point of its original relations the bowel was then divided with the

cautery between the ties A left McBurney incision was made and the proximal loop of colon was delivered through this opening where it was fixed with an Ochsner clamp and also by several sutures to the skin The rectum was then freed from the pelvic wall by blunt dissection just superficial to the periosteum All vessels were isolated, clamped and divided and tied as they were met This dissection was continued down into the pelvis until the levator muscles were reached Then a loop of ileum about 20 cm from the terminal ileostomy was identified and the mesentery of the ileum was divided in such a manner that the terminal anastomoses were not interfered with although the primary branches to that segment of bowel were divided As a result of this maneuver there was now a mobile loop of ileum measuring about 15 cm in length The ileum was then doubly tied with braided silk at its original point of isolation and divided between the ties with the cautery Both the distal and proximal ends were then carefully inverted with purse-string sutures and reinforced with mattress sutures The distal section of bowel was then dropped free into the abdomen The proximal loop was now sutured to the divided end of the sigmoid with mattress sutures of linen after which it was carefully placed in the pelvis to avoid kinking or torsion The abdomen was then closed by two through-and-through sutures and a sterile towel was clipped over the field Then with the patient in the lithotomy position and following routine perineal clean-up with Scott's solution an incision was made posterior to the rectum which was continued forward to divide the rectal sphincter Anal mucosa was then freed from the skin and sphincter muscles Then the levator muscle on either side was identified and divided between clamps Dissection was continued upward until the freed rectum and sigmoid could be delivered into the incision The rectal sphincter was closed with interrupted sutures and the section of ileum was gently pulled down until bowel with good circulation showed through the sphincter The ileum was fixed in this position to the skin margin Two drains were now placed posterior to the ileum up into the pelvis and a tight gauze dressing was applied The patient was then

placed flat on the table again and the abdomen was completely redraped and with another set of instruments the braided silk sutures were severed reopening the abdominal incision The ileum seemed to lie quite loosely in the pelvis and with the patient in high Trendelenburg position the pelvic peritoneum was sutured to the mesentery of the ileum on either side The abdomen was then quickly closed The patient stood the operation exceedingly well She began to show some evidence of shock during the perineal portion of the operation because blood lost had been moderately heavy A transfusion was started at this point and at the conclusion of the operation her condition was fairly good Operation time was about two hours and forty five minutes from the time of the initial incision until the abdomen was closed The purse-string suture was then removed from the old ileostomy stoma and an Ochsner clamp which was closing the terminal colostomy was included in the dressings

Following the operation, the patient had a rather stormy time for a few days but after this she reacted very nicely, began to take fluids by mouth, the pulse improved and her general condition was more satisfactory Several transfusions were given at five-day intervals There was some elevation of temperature in the evening and the blood showed a hemoglobin of 50 per cent but the red count was 4,560,000 About two weeks after the operation, fecal matter began to be discharged from the vagina On examination it was found that the ileum was deficient up to about 1 inch except at one point where it reached the anus and adhered This gave rise to a communication between the large space from which the rectum was removed, and the vagina through a communicating fistulous tract A rubber tube was inserted in the ileum for the purpose of allowing mucosa to grow downward Dilute hydrochloric acid packs in the vagina were used for a while and the space posteriorly was irrigated periodically The patient seemed to be improving slowly but on March 4, 1934, she became very listless, temperature rose to 104° F in the evening, pulse became rapid, she refused to eat and seemed to be failing rapidly This phase lasted for a few days but again she responded in a gratifying

manner to transfusion and intravenous glucose Following this period, she steadily gained strength, the mucosa of the ileum had grown down all around, the posterior space was clean and the communicating fistula with the vagina had healed When discharged, on April 21, 1934, the patient was gaining weight, her general condition was good and three or four formed stools were passing through the terminal ileostomy daily with fair control

She returned to the hospital on May 28, 1934, for observation and possible completion of the operative program During the interval at home she had not been very well on account of constant discomfort around, and frequent discharges of fresh and clotted blood from, the colostomy opening She also complained of pain and discharges from the rectal region She had an evening elevation of temperature since she left the hospital and for the past three days, attempts to swallow have caused marked gagging although she was not nauseated and did not vomit Her mother reports that she has been very nervous and terribly discouraged

The general condition of the patient at this time was fair The blood examination showed her hemoglobin to be 55 per cent, erythrocytes 3,420,000 and the leukocytes 9750 with a normal differential count The urine showed a faint trace of albumin, with an occasional red blood cell, clumped white blood cells in moderate numbers and no casts The anal area was healing satisfactorily and there was some sphincteric control present On account of the picture presented at this time it was thought best to proceed with the final stage of the operative plan Transfusion of 500 cc of citrated blood was given on May 30th and again on June 5, 1934 On June 7, 1934, the following operative procedure was done

After routine preparation of the abdomen with iodine and alcohol, an incision was made through the skin about the terminal colostomy and with strong traction on the terminal colon the bowel was freed sufficiently to invert and close its end The end of bowel was carbolized and treated with alcohol and then covered with a gauze sponge After this the mobilized

terminal colon was pushed back into the abdomen and the left McBurney incision packed with gauze Drapery was removed and again following routine preparation with redraping and change of gloves, gowns and instruments a midline incision was made about 20 cm in length with its center at the umbilicus On opening the peritoneal cavity the abdomen was found to be surprisingly free from adhesions The small bowel was packed over to the right side of the abdomen and with moderately strong traction on the terminal colon, the mesocolon was clamped and divided until it was mobilized to the splenic flexure At this point all clamped tissue was tied and then the abdominal gauze was changed so that a good exposure of the splenic flexure of the colon could be obtained Peritoneal folds were divided between clamps, and the splenic flexure of the colon delivered into the incision Once again all clamped tissue was tied and then the transverse colon was divided from the omentum and from the transverse mesocolon by the clamp and cut method, until the hepatic flexure of the colon was reached The clamped tissue of the omentum and transverse mesocolon was then transfixed and tied At each stage of delivery of the colon a braided silk suture was placed around the freed bowel to control back bleeding The hepatic flexure was then delivered in a manner similar to that used in freeing the splenic flexure, care being taken not to injure the duodenum After the clamped tissue of the hepatic flexure had been tied the ascending colon and cecum were then freed by dividing the lateral peritoneum and clamping the vessels before their division About the cecum a large abscess cavity was found which contained a large amount of thick colon bacillus pus and which seemed to penetrate down into the cavity of the pelvis The mesentery of the small terminal portion of the ileum which was continuous with the cecum was then clamped and that portion of bowel removed All clamped tissue was then tied and then the mesentery of the portion of ileum which had composed the terminal ileostomy stoma was divided between clamps and that portion of ileum was everted through the stoma and divided from the skin Into this right McBurney incision three cigaret drains were placed one of which went

down through the perforating point in the pelvis and which is marked with a suture The other two drains were placed down into the granulating area of the abscess cavity An additional drain was placed down to the abscess cavity from the lowermost end of the midline incision which incision was rapidly closed as above A cigaret drain was then placed down through the left McBurney incision at the site of the old colostomy, after the gauze pack had been removed, and this opening was partially closed with interrupted sutures The patient was considerably shocked during the progress of the operation but her condition improved after receiving 500 cc of citrated blood and she was in fair shape when she left the operating room

Following the operation the patient vomited constantly, extreme hypersensitivity of the abdomen developed, the temperature gradually rose to 105° F and the pulse became rapid and thready Digitalization, intravenous saline and glucose brought only temporary relief Despite the use of cardiac stimulants, oxygen tent, and binding of the extremities, cyanosis appeared, breathing became more and more shallow, spasmodic twitching began, the cardiovascular system collapsed and the patient died on the third day after operation

The following is the report on the operative specimens as described by Dr Vernon H Norwood, the pathologist (The Church Home and Infirmary Pathology No 14642) The specimen received from operation January 30, 1934, consists of a segment of intestine 20 cm in length There is an abundance of fat on the peritoneal surface which measures 3 cm in thickness The mucosal surface shows numerous polypi of varying length up to 1½ cm These polypi are of narrow caliber, averaging 3 mm in diameter being attached by a narrow pedicle The tumors vary in number, averaging at the central end of the segment more than 20 per cm of length The distal end shows cutaneous tags indicating the anal margin The mucosa between the polypi is of a rather edematous appearance but shows no ulceration The muscular layers are of normal appearance

Operation June 7, 1934 (Pathology No [Church Home and Infirmary] 14967) The specimen shows a piece of the large

intestine 112 cm in length, varying in diameter, in the unopened state, from 2½ to 4 cm The fatty tissue of the peritoneal surface is of normal appearance About the cecum tags of old adhesions are found, with an area covered by grayish exudate which suggests the wall of an abscess cavity Attached to the cecum is a segment of ileum 15 cm in length, the cephalad end of which is smoothly sealed off At the time of operation, the segment contained a grayish purulent looking exudate. On opening, however, its mucosa was well preserved and free from congestion, with a normal appearance The mucosa of the colon was rather edematous throughout and had a smooth appearance, except for the polypi similar in size and appearance to those found in the previous specimen They were less abundant, however, being found in greatest numbers in the transverse colon and to a lesser extent in the descending colon The mucosa of the transverse and descending colons was thrown into longitudinal folds, apparently by muscular contraction Polypi were almost completely absent in the ascending colon. No ulcerations of the mucosa and no diverticuli were found

Microscopical Examination — Microscopical sections from both specimens show a similar appearance There is a diffuse inflammatory reaction visible, even in the subserosal tissues and fat which shows a rather sparse distribution of both polynuclear and mononuclear cells, with the former predominating The muscle layers show normal development, and preservation, but the fibers of the inner layer seem somewhat separated as if by an edema Here the same diffuse distribution of inflammatory cells is seen, while between the circular and the longitudinal layers, scattered foci of polynuclear leukocytes are found, which in places tend to assume a perivascular distribution The submucosa is everywhere thickened and fibrotic, with an edematous separation of the fibrous masses in most areas Solitary lymph follicles here and in the mucosa are large and abundant, but there are also many small foci of mononuclear cells of plasma cell type with a slight admixture of polynuclear cells These foci are not especially grouped about the blood vessels The most characteristic changes are

seen in the mucosa which is thickened and irregular The mucosal stroma is edematous and is heavily infiltrated with cells chiefly of plasma cell type The edematous tissue is thrown into elevated folds which in places project as polypi, into which a supporting stroma of submucosa containing greatly dilated blood vessels extends The glands are large showing greatly dilated lumina, often with markedly distorted outlines, somewhat suggestive of the picture of a hyperplastic endometrium Many of these dilated glands are filled with mucoid material and masses of polynuclear leukocytes Much exudate of a similar nature is adherent to the surface of the mucosa The epithelium of the glands is of low columnar type with many goblet cells The dilated glands in the polypoid masses superficially suggest an adenomatous hyperplasia but consideration of the degree of edema, hyperplasia and stretching of the mucosal stroma would suggest that possibly the glands were dilated by the stretching process rather than by an actual intrinsic hyperplasia The diagnosis was subacute colitis with multiple polypi of the mucosa

In summary, the salient features of idiopathic chronic ulcerative colitis are reviewed and an interesting case report presented in which an unusual surgical approach was employed The attempt at total colectomy with terminal ileostomy through the rectal sphincter was made with a full realization before hand of the risk involved The circumstances in the case, the insistence by the patient that life with a fecal cup was not worth living and the presence of multiple polyposis with the ever-present threat of malignant transition justified this radical procedure In this instance the end-result was very unfortunate Perhaps with improvement in the technic this method may prove more successful in similar cases in the future

BIBLIOGRAPHY

Allchin, Sir Wm H Ulcerative Colitis, Proc Roy Soc Med, 2 59, January, 1909

Andresen, Albert F R, and D'Albora, John B The Treatment of Ulcerative Colitis with Special Reference to the Use of Mercurochrome Intravenously, Trans Amer Gastro-enterol Assn, 36 48, 1933

Banks Benjamin M and Bargen J A Relapses in Chronic Ulcerative Colitis Causes and Prevention Arch Int Med., 53 131–139 January 1934

Bargen J A Etiology of Chronic Ulcerative Colitis Jour Amer Med. Assoc., 83 332 1924

Bargen J A and Logan A H The Etiology of Chronic Ulcerative Colitis Experimental Studies with Suggestions for a More Rational Form of Treatment Arch Int Med., 36 818 1925

Bargen J A and Bule Louis A Chronic Ulcerative Colitis A Disease of Systemic Origin Jour Amer Med. Assoc 101 1462 1933

Bargen J A., Brown P W., and Rankin F W Indications for and Technic of Ileostomy in Chronic Ulcerative Colitis, Surg., Gynec., and Obst., 55 196 August 1932

Bargen J A Chronic Ulcerative Colitis Progress in Its Management Proc. of the Staff Meetings of the Mayo Clinic, 9 1–5 January 1934

Bargen J A The Medical Management of Chronic Ulcerative Colitis A Statistical Study of Two Hundred Cases, Trans. Am Gastro-enterol Assn., 30 145–159 1927

Bargen J A. Specific Serum Treatment in Chronic Ulcerative Colitis, Arch Int Med 43 50–60 January 1929

Bargen J A Rosenow E C and Fasting G F C Serum Treatment for Chronic Ulcerative Colitis Arch Int Med 46 1039–1047 December 1930

Bargen J A Ten Years Experience in the Treatment of Chronic Ulcerative Colitis, Trans Amer Gastro-enterol Assn., 49–60 1933

Basler A Med Rec., 80 14 1911 and also Med Jour and Rec., 101 2 1922

Brown T R and Paulson M Chronic Ulcerative Colitis Intern Surg Dig., 8 67 85 August 1929

Brown P W Duodenal Enzymes in Chronic Ulcerative Colitis Med Clin N A 7 9 1923

Brown T R Chronic Ulcerative Colitis Ann Clin Med., 14 425–429 1925

Brust J C M and Bargen J A The Neoplastic Factor in Chronic Ulcerative Colitis New England Jour of Med 210 692–696 March 1934

Bule L A Chronic Ulcerative Colitis Jour Amer Med. Assoc., 87 1271–1274 1926

Crohn B B., and Rosenberg H The Sigmoidoscopic Picture of Chronic Ulcerative Colitis Amer Jour Med Sci 170 220 1925

Dudgeon L S Lancet 1 1006 May 19 1923

Eyre J W H Brit Med Jour 1 100 1003 April 30 1904

Felsen Joseph Intestinal Oxygenation in Idiopathic Ulcerative Colitis Arch Int Med 48 819 November 1931

Felsen Joseph A Practical Ethological Pathological and Clinical Consideration of Intestinal Ulceration Amer Jour of Dig Dis and Nutrition 1 9 July 1934

Gemmel J F Idiopathic Ulcerative Colitis London Baillière Tindall and

Jordan, Sara M, and Kieffer, Everett D Surgical Treatment of Ulcerative Colitis, Trans Am Gastro-enterol Assn, 61–69, 1933

Kuttner, L Zum Kolitis Problem, Deutsche Med Wochenschrift, 52 1762, October, 1926

Luesden, J T Observations on Colitis Ulcerosa with a Contribution to the Knowledge of the Pathogenic Effects of Colon Bacilli, Nederl Tijdschr v Geneesk, 2 2890–2905, 1921

Logan, A H Chronic Ulcerative Colitis A Review of 117 Cases, Coll Papers Mayo Clinic, 10 180–202, 1918

Lynch, J M, and Felsen, J Tumors of the Colon and Rectum, P B Hoeber, New York, 1925

McGarrison, R Studies in Deficiency Disease, London, H Frowde, Hodder and Stroughton, 1921

Mackie, T T A Bacteriologic, Roentgenologic and Clinical Study of Ulcerative Colitis, Amer Jour Dig Dis and Nutrition, 1 466, September, 1934

Mackie, T T, and Gaillard, Mary, S B Southern Med Jour., 27 492–499, June, 1934

Mummery, P L Brit Med Jour, 2 1685, 1911, 1 497, 1920

Nabarro, Quoted by Hurst, A F Brit Med Jour, 1 693–694, April 25, 1931

Paulson, M Chronic Ulcerative Colitis with Special Reference to Bacterial Etiology, Nelson's System of Medicine, Thomas Nelson & Sons, New York, 28 50, 1929

Paulson, M Chronic Ulcerative Colitis with Reference to a Bacterial Etiology, Arch Int Med, 41 75–94, January, 1928

Rankin, Fred W Multiple Polyps of the Colon, Southern Med Jour., 27 574–578, July, 1934

Rolleston, Sir H Lancet, 1 939, 1923

Rosenheim, Theodor Ueber Colitis Gravis, Deutsche Med Wochenschrift, 52 1764, October, 1926

Satterlee, G R Amer Jour Med Sci, 164 313–322, 1922

Saundby, R On Epidemic Sporadic Dysentery (with Shiga's Bacillus) in England, Brit Med Jour, 1 1325–1329, 1906

Smith, C E The Pathology of Colitis, California and Western Medicine, 23 1311, October, 1925

Soper, Horace W Ulcerative Colitis, Trans Amer Gastro-enterol Assn, 30 160–171, 1927

Stone, H B Surgical Treatment of Chronic Ulcerative Colitis, Ann Surg, 77 293–298, 1923

Torrey, J C Bacteriology of the Human Colon with Particular Reference to Ulcerative Colitis, Trans Amer Gastro-enterol Assn, 1927, 30 129

Thorlakson, P H T Ulcerative Colitis, Canad Med Assn Jour., 19 656–659, 1928

Vedder, E B, and Duval, C W Jour Exper Med, 6 181, 1901–1905

Virchow, R Die krankhaften Geschwulste, Vol 3, Berlin, A Hirschwald, 1863–1867

White, W H On Simple Ulcerative Colitis and Other Rare Intestinal Ulcers, Guy's Hospital Reports, 45 131–162, 1888

Wilks, Sir S., and Moxon Lectures on Pathological Anatomy London J & A Churchill, 1875

Winkelstein A New York State Jour Med., 31 1400–1402 November 15 1931

Young H H Canad Med Assn Jour., 12 332–333, May, 1922

Young H H The Sterilization of Local and General Infections Experimental and Clinical Evidence of Results Obtained by Intravenous Injection of Mercurochrome = 220 Soluble Jour Amer Med Assoc., 87 1366–1372 1926

Zweig Walter Repetitorium der Darmkrankheiten Deutsche Med Wchnschr., 55 918–919 May 1929

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR ESTHER L RICHARDS

THE JOHNS HOPKINS UNIVERSITY

BEHAVIOR PROBLEMS OF THE PEDIATRICIAN

THE behavior of children is a topic that has never given physicians much concern, except as it interfered with the child's taking of medicine, or remaining in bed or submitting to physical examination The contributions of psychology to the behavior of childhood have aroused little medical attention because of the traditional beliefs that the mind of the child belonged to the clergy and teacher, and the body of the child was the doctor's province The effect of states of mind on bodily conditions in children has not until recent years attracted medical attention because physicians have not been interested in mind body relationships in either grown ups or children This failure to recognize the practical value to the practitioner of a working knowledge of how mental strains register in "nerves" and badness of childhood has closed to the doctor a wealth of helpfulness which he alone is capable of giving to parents and teachers Badness has been considered purely as a matter of ethical moment, and not as a matter of scientific interest in why the child behaves as he does In like manner, "nerves" which have been for years a dark chapter in medical science with grown ups have been thought of in equally obscure terms as they appear in childhood 'Nerves" in grown up and child are wont to be thought of by the practitioner as little white strings which come down from the brain and out to the body and need to be tightened with fresh air and rest and food and tonics just as the violinist tightens the strings of his instrument to bring out better harmonies Now nerves do look like little

white strings when one dissects them, and when the physician comes upon them in their handicaps of infantile paralysis and Little's disease and conditions of intracranial pressure with or without convulsive manifestations On the other hand, the behavioristic component of nerves is something which appears in the child's total behavior and something which cannot be evaluated and treated in terms of a lesional pathology Nerves and badness are of scientific interest in that they represent the strains of environmental influences on constitutional endowments poorly adapted to meet these strains As physicians we have grown to teach the layman to ask whether "nerves" and badness are the result of heredity or environment Our real job is to teach parents and teachers and ourselves to ask in any given problem of "nerves" and "badness" the following questions

1 What kind of constitutional stuff—intellectual, biological and temperamental—is this child or adolescent made of?

2 What environmental and educational process offers any given constitutional endowment its best chance of growth and development?

In arriving at answers to these questions we can avail ourselves of two groups of facts First, the facts obtained from the tests of life which represent the way any given child and adolescent has reacted to the environment of home and group contacts and the passing of grades in school Second, the manner in which any growing organism reacts to scientific tests of intelligence and physiologic functioning We have no scientific tests for emotional adaptation

The physician in the past has not thought clearly along these lines, but has had a vague idea that if you could get a child through teething and acute infections and on the school towpath this child would somehow or another come out all right in the end, especially if he got past that monumental guidepost known as puberty The medical mind has very imperfectly realized what a great variation there is in the developmental possibilities of childhood Until the intelligence test was put together in 1911 the only intellectually backward child that the

physician knew about was the idiot and imbecile whose vacancies were so apparent in dropping jaw and empty eye that medical science diagnosed the condition by the inspection of one swift glance. The intelligence test which is one of the great outstanding contributions to child health of our century has discovered for us a wealth of variation in child and adolescent intellectual capacities existing in human material which looks perfectly well put together on the outside. For example, intelligence tests show us, at a conservative estimate, that 25 per cent of school children are mentally retarded—*i. e.*, that no matter how much intensive education they are exposed to they can never develop intellectually beyond eight to twelve, or twelve to fourteen years of age. Looking at the bodily configuration of these individuals one may easily think that they fail in classes and lag behind their fellows in other ways because they are lazy and do not try. The first group is not even junior high school material. They demand a special type of educational process of opportunity class, vocational class, and other modifications of the regular curriculum after they reach that point in their school career when they can go no further because they are beyond their intellectual depth. If parents and teachers force these boys and girls beyond their intellectual capacities the victims of this forcing process will do one of two things, according to their temperament. If they are outgoing, aggressive, energetic organisms, they will seek satisfaction and enjoyment in some other place besides school, recruiting the ranks of truancy, and eventually drifting into delinquency. If they are of a shy, ingrowing, sensitive docile temperament, they will brood over their failures, retreat more and more into themselves, and eventually develop a wealth of nerves with a wide variation of symptomatology. In other words, 'nerves" and "badness" may represent the strain of a Mack truck load of teacher and parent ambitions and strivings thrust upon a Ford chassis of constitutional capacities. The first step then when the physician is confronted with poor mental and social health in his young patients is to go about a logical scientific diagnosis of why the individual behaves as he does. If he cannot estimate the intelligence

capacity himself, he should send the child to some psychological clinic which can do it for him The public is rapidly getting out of that period when they will long remain satisfied with medical platitudes that Mary is too nervous to stay in school, and must be taken out until puberty, that if the parents would only get busy and understand John all would be well The only treatment is to ascertain John's intellectual capacities first of all and see whether he is being pushed beyond his depth Head aches, vomiting, palpitation, crying spells of one sort or another, irritability, truancy, stealing, sex experimentation are a few of the symptomatic bodily and temperamental protests which the growing organism puts out against strains of life which are too great for him to meet as a so-called "average child" and "adolescent" are expected to meet them The physician can no longer trust even the most expensive, socially exclusive and intellectually "high-brow" private school to give an adequate opinion on a child's intellectual capacity unless that opinion is backed up by a psychological and an educational performance test Too many private schools force parents to tutor their offspring winter and summer as part of a forcing system with college and university as its goal Having discovered the intellectual incapacity the only wise and safe procedure is to take a firm stand and point out clearly to parents, and if need be to teachers, that the child's mental health lies only in relieving him from having to be forced to keep up to educational standards beyond his capacity, and to urge that he be given an opportunity to grasp other educational processes that are suited to his handicaps

There is a second constitutional endowment which the physician is continually called upon to treat, and that is the handicaps of what we might speak of as a neuropathic constitution Such children are born with a different biological endowment than their fellows They are frequently of an asthenic habitus—lean, skinny, small-boned, prone to catch every infection, hypersensitive not only to foreign proteins, but to strains of environmental situations and the pushing of competitive struggle in school life As protests against these strains they

are wont to develop a wealth of symptomatology—rumination in infancy, eczema, bed wetting night terrors, stammering, asthma tics choreiform manifestations, mucous colitis, attacks of pylorospasm, spastic colon, not to mention seizures of shaking and trembling and "going all to pieces" We have no so-called "pathology" to account for these symptoms Sometimes the organism may show protein sensitivity, and sometimes it does not In the majority of cases the intellectual equipment is average and even precocious The temperament is as a general thing high strung, sensitive, edgy, intense Here are children and adolescents who require much more sleep than the average biological endowment, who cannot attain weights that are ideal on charts for their height and age, whose whole biology is as mercurial as their temperament In short, they seem to be put together the wrong way from a nervous system standpoint, and there is nothing we are able to do about it Perhaps it is their autonomic nervous system which is at fault Be that as it may, no power of medical science can make them over, and our job is first of all to recognize their constitutional biological limitations, and second to teach them early to live with these limitations without trying to make themselves over From the school standpoint they are very frequently mismanaged because their eagerness to please and their energy and their good intellectual equipment intrigues the school into encouraging them to skip grades, to take prominent parts in public exercises, to compete for prizes and awards which keep them continually stirred up in a state of emotional unrest It is not enough to worry them during the school year but they must be put through the mill of music lessons, dancing classes and summer camps, where they are again exposed to competitive struggle in athletics and social prowess It is useless to treat an asthmatic child with serum when he is exposed to an environment that never allows him to relax On the other hand equally important with the serum is medical insistence on the child's being taught good habits of emotional control The asthmatic child for example, is so pitied by his parents and doctor and teachers that he is allowed to have his own way in every detail lest he get an attack

of asthma Wittingly or unwittingly he drifts into the habit of utilizing his neuropathic tendencies to wheezing, or coughing, or vomiting to control environmental situations and get what he wants The result is a vicious circle which can only be broken by the physician's attacking the behavior problem frankly, and insisting that this child be taught the same principles of social responsibility for the rights and privileges of those around him that his non-neuropathic fellows are obliged to follow Here again it is futile for the physician to hand out platitudes about waiting till age brings about a change in behavior There is no magic about puberty or adolescence that will make over the spoiled behavior of a neuropathic child In fact age brings with it the momentum of increasing energy and increasing emotional urges Making allowances for the temperamental annoyances of the neuropathic child with the therapy of temporizing merely postpones the day when society and the world of wage-earning and family formation and group life demands that the neuropathic fits into the social group just as any other person In short, the training of such a child, or adolescent, in learning his limitations of fatigue, and competitive striving, and in learning early to manage his instincts and emotions cannot be begun too early To neglect it may give us on the one hand a life-long nervous invalid, and on the other hand a petulant, eccentric, explosive grown-up who is a source of misery to himself, and a nuisance to all with whom he is associated

A third point of differentiation of the constitutional stuff out of which the child is made has to do with the temperamental equipment, or disposition Temperament, or disposition, is a matter which our profession has been wont to leave to religious education and schools We have had the notion that one kind of temperament could be easily converted into another through a little effort We have not realized the serious importance of the temperamental set-up with which we are born Psychology is telling us that roughly speaking we may divide temperamental endowments into two groups—the outgoing and the ingrowing The outgoing temperament is one whose emotions and instinctive performances are quite objective You see the flare-

up of anger, the outburst of tears, the expression of joyousness with all their modifications, plus, or minus, as they are expressed in the words and actions of their owners It is a kind of temperamental equipment which lends itself readily to modification all the way along We can teach, or try to teach, the child how to control his anger and not strike out with his fists We can teach him how to tone down his ecstasy and modify his sulking and down heartedness On the other hand, when we come to deal with the ingrowing temperament we are baffled because we cannot get at its manifestations It is shy, docile, quiet, timid, not assertive, uncommunicative and prone to get its emotional satisfaction not out of the world of reality so much as out of the world of phantasy and daydream It is so sensitive to the rough give and take of social contacts that it cannot meet them and take part in them, and therefore retreats into disguising expressions of its real emotions It does not care for play or mixing with others, and therefore it early develops a feeling of inadequacy in human relationships Coupled with this anaerobic disposition is usually a strong undercurrent of conscientious striving which keeps the personality ill at ease Such a child and adolescent does not give home and school much trouble because it is not forever trying to register itself on the environment Therefore environment takes the individual for granted and goes along molding it according to respective standards of what it should do and be Teachers find such a child a joy in the classroom because it tries hard and is never a disciplinary problem In like manner parents regard such a boy or girl as the easiest one of the flock to raise because it never gives them a moment's anxiety It does not steal, or lie, or fight, or break windows or run away, or play truant. It is a good child But as the years pass no one knows what is going on in the growing organism's mind till under the strain of some pressure of school, or social or vocational standards against which the individual makes no objective protest the growing creature begins to grow more seclusive, stand-offish, asocial and perhaps plain queer At this point in its life the damaging processes of the ingrowing personality are frequently de-

veloped beyond the point where they can be modified Habits of food and recreation drop out Lassitude appears The adolescent sits about or stays in bed longer and longer, and gradually ceases to display active interest in the world going on about him Tonsils are removed, teeth are straightened, glands rejuvenated, and calcium administered without avail It is over just such thresholds of unrecognized and misunderstood personality endowments that the dementia praecox reaction puts in its appearance The mental hygiene treatment of such a condition must involve an early recognition of the temperamental ingredients of the endowment Parents and teachers must not go along taking these temperaments for granted, but must early adopt ways and means of trying to draw out the child in play and social contacts little by little toward a goal of early establishing *in him a sense of enjoyment in his contacts with others* Our systems of play from nursery school on are too much concerned with featuring play for the few who excel in its activities and thus shed glory upon the school body Even the most advertised private school rarely ever considers a play life for every child, or sees to it that he is studied as carefully from this aspect of his educational process as he is from purely academic standpoints Science finds it more or less impossible to make an ingrowing temperament outgoing But it can teach us how to make both temperaments more aware of their respective possibilities for a reasonably all-around personality development

In the foregoing paragraphs the writer has tried to set forth a few principles underlying a logical and commonsense scientific approach to an understanding of childhood activities as behavior in contradistinction to judgment passed upon them as conduct With these principles in mind the physician can arrive at some sort of guidance in his practice, and at the same time he spared the complexities that now confuse the field of psychiatry by reason of its youth Psychiatry is a branch of departmental knowledge that is struggling to find order out of the chaos of several different points of view which claim to be panaceas for all behavioristic ills There are the endocrinologists who would have us believe that behavior is the sum total

of glandular balance, and that if we could but find the key to polyglandular harmony childhood would start on the road of perfection And there is the school of psychoanalysis that would have us believe that eternal salvation in the sphere of human relationships lies in capturing the vagaries of the libido And there is yet another school which would have us put our faith implicity in foci of infection, maintaining that all aberrations of human behavior have their source in pus somewhere in the system We should strive in our stable thinking to render unto glands and libido and focal infections and habit training and constitutional endowment and environment the things which in each individual case offer us helpfulness in any direction But we shall fail to see the forest because of the trees if we dedicate our thinking exclusively to any one point of view Plants and animals can be depended upon to develop with reasonable evenness from seed to flowering maturity, but the human being is far too complex in his organization to be depended upon to develop according to set patterns which any scientific theory lays down for him It is therefore unwise to classify children any more than grown ups into groups of normal and abnormal It is only when we think in terms of varying degrees of normality that we become constructive in our diagnosis and treatment

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR. ROBERT W JOHNSON, JR

CHILDREN'S HOSPITAL SCHOOL

ARTHRITIS IN CHILDREN

IN discussing arthritis, whether it be in adults or children, we must always recognize that arthritis is a broad term covering all forms of joint irritation and inflammation, and is, therefore, quite vague and indefinite when used alone Arthritis merely denotes a joint lesion, and we do not give it diagnostic value unless we qualify the term "arthritis" by some specific adjective of etiologic character, such as tuberculous, luetic, etc. When dealing with clinical material let us try to be equally honest with ourselves and our patients, and refuse to give or accept arthritis as a diagnosis without qualifying it as accurately as our science or skill will permit Tumor albus and coxalgia no longer satisfy us though sixty years ago they represented as complete a diagnosis as the clinician of that day could offer Some of our present clinical diagnoses may seem nearly as crude within the next half century Rheumatism with its honest vagueness seems to me preferable to arthritis with its pseudoscientific Grecian itis just as white swelling and hip disease were better than their Latin counterparts

In the study and treatment of the arthritides we have made great progress to date but there is much yet to be solved, and unless we maintain a lively dissatisfaction with the state of our knowledge advances will be slow Having made our preliminary point on the general subject of arthritis, let us examine the factors making the joint diseases of children a rather different problem from adult arthritides

1 **Congenital Defects and Abnormalities.**—The presence of these in children give rise to a type of joint change not met with in adults except in the final stages As examples of this let me cite two dissimilar conditions

(*a*) Congenitally dislocated hips which cause a wandering of the acetabulum or new socket formation in the ilium and distortion of the femoral head which lead to gradually increasing irritative reaction and a true mechanical arthritis

(*b*) Hemophilia, in which the acutely painful and blood-filled joints suffer permanent damage and pathologic lesions soon demonstrable even in *x*-ray Though not a deformity this inherited diathesis falls into the congenital group of arthritis

2 **Nutritional Disturbances**—These play a great rôle in childhood and get less important as growth wanes and maintenance demands are all that have to be provided for Scurvy primarily and rickets secondarily affect the joints and their function Acute or chronic joint irritation and disability follow in the wake of these two important nutritional diseases The results of them not uncommonly reach a point where even pseudoparalysis is seen

3 **Growth**—The growth processes active in childhood make the bony structures entering the joint more plastic than in adult life So they give rise to a group of epiphyseal or growth disturbances with joint manifestations, such as Legg-Perthes disease, femoral epiphysiolysis, Kohler's disease, spinal epiphysitis, etc This is a most important group to isolate from the general indefinite mass of arthritides and a group limited to childhood

4 **Directly Inherited Disease**—Lues is the outstanding example of this Congenital syphilis with its great affinity for the bones and joints in infants and children presents a clinical group of prime importance, while in the adult the bone and joint lesions of acquired lues are much rarer and relatively benign

5 **The Prevalence of Acute Infectious Disease in Childhood**—This factor coupled with the relatively low resistance of children accounts for the greater incidence of acute pyogenic arthritis in children—streptococcal, staphylococcal and

pneumococcal In fact the only acute joint infection seen more often in adults than in children is the gonococcal, the reason of which is obvious

6 **The Mode of Life**—A child lives under very different conditions than does an adult The baby in the crib with an infected caretaker, or a small child crawling about the floor and putting objects found there in its mouth, can pick up overwhelming infections that an adult would escape in the same surroundings This accounts for the large incidence of tuberculous arthritis in children as compared to adults The soil is virgin and rich, the seed profusely sown so the harvest of ill is early and abundant

The above six categories deal with factors favoring the incidence of certain specific kinds of arthritis in children Let us now reverse our point of view and seek out factors absent in childhood which serve to make adults susceptible to other specific varieties of joint change In considering arthritis in children one can automatically eliminate from consideration the following types of arthritis quite commonly seen in adults

1 **Degenerative changes** resulting from senescence or prolonged wear and tear, of which the very common and outstanding example is hypertrophic or osteo-arthritis

2 **Metabolic disturbances** such as gout and osteomalacia

3 **Neurotrophic degenerative lesions** of syringomyelia and tabes—the Charcot joint

4 **Neoplasms**—The neoplasms of childhood are diaphyseal conditions scarcely ever involving the joint while both primary and metastatic neoplasm are found in the joints and spine in adult life

However it is not among those cases of arthritis in which the etiologic factor is readily discoverable that the chief diagnostic and therapeutic interest lies In children, as in adults, it is the obscure and unknown that both challenge and fascinate us Therefore, let us pass on from the cases in which our clinical and laboratory tests can establish the causative factor, for in them the road to therapy is well marked by the sign posts of the written text and the footprints of our predecessors and

colleagues Rather let us turn into the wilderness of arthritic cases whose cause and treatment are still vague, and speculative, and try to find what light we can to guide us through its dim twilight It is fatal to the successful handling of arthritics to try to pigeonhole cases of this vague group into neat compartments and subject all cases in the same compartment to the same therapy or régime, a procedure much too frequently attempted Salicylates may give a measure of relief to most cases of this type, but that does not mean that the cases are all alike The psychiatrists who use sedatives in most of their cases do not lose sight of the fact that each mental case is a distinctly individual problem The same absolute individuality is true of arthritics Therefore, while we may find certain titles convenient, such as Still's disease, infectious arthritis, etc , let us keep our heads clear and be analytical enough to pursue an individual course for each patient

A few case abstracts might serve to illustrate this diversity to be found in arthritic children, and explain why one must acquire experience and yet retain elasticity in dealing with such problems

Case I—V H , white female, aged eight years Admitted to Children's Hospital School, March, 1930, discharged August, 1933

Diagnosis—Still's disease

Family History—Negative

Past History—Negative to onset of present illness except measles and whooping cough Also had injections against scarlet fever

Present Illness—Onset at four years of age with pain and swelling in metatarsophalangeal joints of right foot Next left wrist and then left foot and right foot became similarly swollen and tender Slight daily temperature elevation Constipated Continued up and about

Tonsillectomy and adenoidectomy done for possible focal infection shortly after onset of disease, 1926 No effect

November, 1929, had extension of process to knees with

pain, and child became bedridden and knees contracted Neck became sore and stiff also

Treatment prior to admission (1) Tonsillectomy and adenoidectomy, (2) vaccine from organisms cultured from stool, (3) "glandular" vaccine, (4) osteopathy—massage and light

Fig 184—Case 1 Fusiform swelling of many joints—muscle atrophy Control of deformity by splinting

Physical Education—Poorly nourished Fingers, wrists feet and knees swollen tender and contracted No redness and only slight local heat over joints Head nose and throat teeth neck and lungs negative Heart negative Abdomen—liver palpable, not enlarged Spleen not palpable Moderate general glandular enlargement

Hemoglobin, 75, white blood corpuscles, 7500 Temperature 99 2° F

Skin sensitization test done with mild positive reaction to one strain of nonhemolytic streptococcus, later used for vaccine

Treatment—Rest Dietary upbuilding Cod liver oil, etc. Splinting and traction for contracted joints Massage, active and passive motion to stiffened joints Hydrotherapy

Vaccine therapy to strain to which she was mildly sensitive

Excision of gland for culture negative

Protein shock and desensitization

Heliotherapy and carbon arc light

Colonic irrigations and supervision of elimination

Progress—Slow progress of the arthritis so that despite temporary improvement from time to time patient was discharged in worse condition than on admission and was taken into the "Home for Incurables"

Discussion—All efforts directed against the disease failed in this case as did all efforts to build up resistance of the patient, and the course was a slowly downhill one There were few leads in the history and physical findings gave little indication as to cause or mode of therapy Not a true Still's disease in that sudden exacerbation and temperature flares were absent A brand that could not be saved from the burning

Case II—T M, white female, aged two years Admitted March, 1927

Family History—Negative

Past History—Negative except for otitis media at one year

Present Illness—Onset nine weeks ago Coryza, convulsions, fever and restlessness Admitted Johns Hopkins Hospital Nasal discharge, cough, purulent conjunctivitis, draining ear Temperature 100 4° F Semicomatose Cervical rigidity Kernig positive

Diagnosis—Tuberculous meningitis? Otitis media?

Spinal fluid proved clear and symptoms subsided, but left knee joint swelled and patient crawls instead of walking Transferred to Children's Hospital School

Physical Examination—Vision poor Head, neck, nose and ears negative Heart and lungs normal Abdomen negative Spine and extremities negative except for knees Both knees swollen with flexion deformity Tender to touch and motion No local heat. Fluid plus, plus Synovia plus, plus, plus Temperature 99 –100° F

Treatment—Rest with traction to overcome deformity Later physiotherapy as inflammation subsided General up building measures

Later had acute tonsillitis with slight increase in arthritis

After four weeks interval tonsillectomy and adenoidectomy performed August 10, 1927, and discharged home cured, September 4, 1927

No recurrence Patient followed in Johns Hopkins Hospital Dispensary

Discussion—Acute illness with residual joint symptoms clearing slowly as patient's general condition improved Recurrence with acute tonsillitis Later removal of tonsils and adenoids with entire cure of arthritic symptoms

Case III—N H, white female Admitted, March, 1932

Family History—Negative

Past History—Entirely negative up to present illness

Present Illness—At age of four years she began to have joint pains and knees became swollen Then phalangeal joints and wrists were involved Always poorly nourished Exacerbations and remissions but never freedom from symptoms in eight years Often bedridden because of pain Spent four years in California for climate Tonsillectomy and adenoidectomy done at seven years

Physical Examination—Tall very thin Color pale. Intelligent Knees, ankles, wrists and hands show fusiform swelling with muscle atrophy Swelling synovial not fluid Cervical spine stiff No foci of infection found on physical examination Cultures of stool showed coli and streptococci Throat Pneumococcus Nose Staphylococcus Wassermann test

negative Agglutinations Negative x-Rays negative Hemoglobin, 80 White blood corpuscles, 10,000

Treatment—Rest High caloric diet and vitamins
Heliotherapy and carbon arc
Excision enlarged inguinal gland for culture—negative
Skin sensitization—agglutinations repeated
Slight sensitivity to nonhemolytic streptococcus strain
Intravenous vaccine therapy No appreciable result or reaction except feeling of improvement

Gain in weight and general appearance improved, with joints less swollen and tender, but still showing arthritic changes

Course has been followed for three years with occasional flare-ups when overfatigued, necessitating several rest periods of a fortnight from school In October, 1934, had acute appendicitis requiring operation and has not regained weight or physical reserve since Requires more rest and is out of school temporarily, but arthritis has not been unduly active

Discussion—In this case general upbuilding and protection from overfatigue has enabled this patient to arrest and really overcome a long-standing arthritis of undiscoverable etiology A case bordering on the true Still's disease which has made gratifying progress

Case IV—G S, white male, aged eleven years Admitted April, 1927

Family History—Negative

Past History—Influenza at two years, quite ill Two attacks of otitis Infrequent colds No sore throats Heart, lungs and gastro-intestinal tract negative

Present Illness—At seven years of age had diphtheria and has not been well since Joints sore and had to limp from time to time Six weeks prior to admission was thrown on back in play and stayed home two to three days Some pain, but only in past two weeks too bad to walk Kept him awake at night. Stiff after resting Night cries Limps and drags left leg a little

Physical Examination—Well nourished Acute pain in

lower back on moving in bed Tends to lie on abdomen Head, eyes, nose negative Pharynx injected Tonsils not large Heart, lungs and abdomen negative General glandular enlargement Tender over left sacro-iliac Kernig's and Goldthwait's signs plus, plus, plus Temperature normal White blood corpuscles, 9200 Hemoglobin, 82 per cent.

Impression—Tuberculous left sacro-iliac

Treatment—Tuberculin tests negative *x* Rays negative Use of salicylate gave temporary relief

Diagnosis—Subacute infectious arthritis left sacro-iliac

Course—Tonsillectomy and adenoidectomy done after complete study of case Complete disappearance of arthritis with no recurrence in eight years

Discussion—Early case where tuberculosis was suspected, definite relation to severe diphtheria and throat infection quite obvious Improved under upbuilding regime and cleared up completely with removal of a single focal infection.

Case V—V M, white female, aged five years Admitted May, 1922

Family History—Negative

Past History—Otitis at four years Nose and throat negative Chest and abdomen negative Bowels regular Genito-urinary negative

Present Illness—One year ago sudden soreness in one knee, clearing in a few hours but recurring for four days Knee swollen

Diagnosis of tuberculous knee made at hospital in New York Cast applied Four weeks later other knee swelled Taken to a crippled children's hospital and put in traction No improvement and patient admitted to Children's Hospital School, for study of arthritic condition

Physical Examination—Thyroid slightly enlarged Child nervous Chest heart and abdomen negative No general glandular enlargement Boggy swelling and tenderness both knees Local heat plus No redness Motion 180–120 degrees

Tuberculin test negative Blood Wassermann negative Temperature 99 2° F

Treatment—Tonsillectomy and adenoidectomy done No improvement in knees noted

Readmitted August, 1922, with beginning involvement right hip No foci found Gland excised and cultured Autogenous

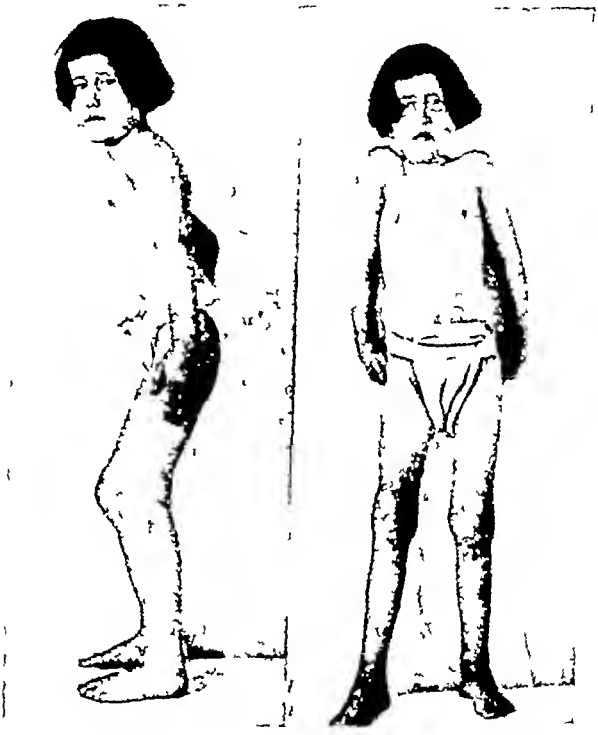


Fig 185—Case V Old joint changes and contractures

streptococcus vaccine given without noticeable improvement during next ten months Right wrist became involved

Lost sight of when discharged, as family moved away Seen five years later on visit Had been in a children's hospital in midwest city Had colectomy done for arthritis and various vaccines, etc , given Slow progress

Seen again 1932 Large, well-grown girl with mild hyperthyroid signs Arthritic process had progressed, but was not

active at that time Considerable residual damage to knees, wrists and several fingers Able to attend school Seen again 1934, with slight flare-up due to overwork at high school and long trip to and from school Rest and instructions against overwork and worry served to cause subsidence of symptoms Still hyperthyroid, but will do nothing about it

Discussion.—Valuable time lost in treatment for one year for tuberculosis Infectious process established Later tonsillectomy and adenoidectomy and colectomy not effectual Value of vaccine therapy debatable Late recognition of an endocrine factor which might have been important early and which is certainly an active factor at this time Permanent damage despite care, but patient saved from much more severe disability than would probably have occurred

CONCLUSION

It has been my purpose to show that there is no royal road to success along which the doctor can point his patient, but rather a toilsome exploration of byways and blind alleys and obscure paths with doctor and patient going along hand in hand until at last the wilderness is passed through, and the pleasant fields of health and activity discovered on the other side

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR HENRY M THOMAS, JR

THE JOHNS HOPKINS HOSPITAL

THE PRESENT STATUS OF VITAL CAPACITY AS A TEST OF PULMONARY EFFICIENCY

SINCE 1846 when Hutchinson published his studies on some two thousand individuals made with a spirometer, which was water sealed and with a counterpoised bell which he devised and which is practically the same as the one in general use at the present time, vital capacity has been a determination of interest and use in clinical diagnosis Hutchinson realized that many normal variations in physical make-up alter the volume of the vital capacity and his and most of the subsequent studies have attempted to establish physical measurements by which the expected vital capacity of any given individual can be estimated Dreyer, in recent years (1920), has made extensive observations along these lines and has elaborated very complete tables for men and women of all ages and sizes and has further subdivided them into three groups according to their degree of physical training and habits of physical activity Meyers reviewed the literature on this subject (276 references) very completely and reported it along with his own work in a book published in 1925 This serves as a summary of much of the important work on vital capacity up to the time of its publication Particularly helpful is the chapter on Normal Vital Capacity Standards in which he reviews the data presented in favor of each of the possible normal standards i e standing height body weight surface area, sitting height (stem height) and chest circumference He publishes tables for men and for women with each of these standards whereby an individual's vital capacity may be compared with the normal and suggests as most satisfactory those based on surface area, weight

or standing height These tables do not allow for normal variation produced by occupation but he states that if one wishes to follow Dreyer in this respect one may deduct 8 7 per cent from Class A (athletes or persons in excellent physical training) to obtain figures for Class B (professional men, business men, railway men, high grade mechanics and clerks of the upper class) and 14 6 per cent for Class C (tailors, shopmen, shoemakers, printers, potters, clerks of the lower class and painters) Obesity and old age cause reduction in vital capacity, Chinese and Negroes have lower vital capacity than members of the white races and in the recumbent position the vital capacity is 5 per cent lower than in the standing position From these facts one sees that even the most elaborate standards of normal vital capacity as estimated from body measurements, age, sex and race are only approximate

Many studies have been made of the reduction in vital capacity caused by disease mainly of the chest wall, lungs or heart In heart failure the vital capacity runs roughly parallel to the dyspnea and the clinical condition of the patient (Peabody) and this fact may be utilized in differentiating effort-syndrome from true heart failure (Adams and Sturgis) and true from false dyspnea (Levinson) It is also a useful guide in demonstrating graphically improvement in cardiac power (Pratt) The reduction in vital capacity (shown by Peabody and others to occur) in hyperthyroidism is thought (by Lemon and Moersch) to be due to the cardiac inefficiency which arises from the primary source, the thyroid In pneumonia the degree of reduction in vital capacity does not parallel the amount of lung involved, and four-fifths reduction may accompany consolidation of only one lobe Asthma, emphysema, bronchitis, pleurisy, pneumothorax, pulmonary abscess, bronchiectasis and new growths all cause a reduction in vital capacity, and pulmonary tuberculosis has been studied extensively by this method Recently attention has been redirected to emphysema and pulmonary fibrosis also is being carefully investigated (McCann)

In short, vital capacity is a measure of the impairment of either respiratory or circulatory function although from studies

of the vital capacity alone little insight into the different causes may be gained Mechanisms producing reduction of the vital capacity are, many of them, obvious, such as limitation of move ment of the chest wall by bandages or by pain from pleurisy, and diminution of lung volume by pleural effusion or by bronchial obstruction In heart failure, however, congestion and stasis in the pulmonary capillaries and small vessels has been shown both to encroach upon the alveolar spaces and to interfere with the elasticity of the alveolar walls (Siebeck, Christie) "Em physema," writes Meyers, 'unquestionably reduces the vital capacity of the lung" and he should have added that Siebeck and others have pointed out a coincidental increase in residual air In emphysema not found in most other conditions in which reduced vital capacity occurs Pulmonary tuberculosis causes a reduction according to the degree of activity of the process Physical weakness and fatigue have been shown (Peabody) to play only a small and insignificant rôle in reducing vital capacity

In the past few years there has been a very marked increase in the interest taken in perfecting tests for pulmonary efficiency and nearly all include the determination of vital capacity Note worthy among the work in foreign clinics is that from Brauer's in Hamburg, Germany, by Anthony and others, and Moncrieff has continued the work he began there since his return to London He gives a brief resume of the tests for respiratory functional efficiency and reports the results of 86 cases studied by the methods he considers likely to produce valuable in formation He divided the cases into 6 clinical groups accord ing to the amount of dyspnea present and compared the results obtained by the following tests (*a*) Vital capacity, (*b*) dead space, (*c*) ventilation equivalent for oxygen (*d*) length of ex piration, (*e*) mercury U tube test

It is not the place in this paper to enumerate the various technical aspects of these tests Suffice it to say that out of a good deal of controversy in regard to test (*b*) the dead space (which exists in the air passages above the bronchioles), there emerges the opinion that the 'functional' dead space increases

with the depth of respiration and also as the lungs become less efficient as an organ for introducing oxygen into the blood and removing carbon dioxide from the blood In this and a previous paper, Moncrieff attempts to correlate the increase in dead space with the reduction in respiratory efficiency of the lungs From his figures it is apparent that there is a rather rough correlation but the coefficient of variation was obviously large, the average change small compared to the amount of functional disability and the technical difficulties of the test too great for ordinary use By ventilation equivalent for oxygen (Anthony) (test (*c*)) is meant the volume of inspired air, in liters, that gives up 100 cc of oxygen to the body The normal was found to be 2 5 liters ± 0 522 which remains unaltered after forced breathing or moderate exercise It is greatly altered, however, by a change in the CO_2 or O_2 content of the inspired air or by changes in the CO_2 or O_2 combining power of the blood This test showed no useful correlation with clinical disability nor did the remainder of the tests studied by Moncrieff with the exception of vital capacity and this, the oldest of all tests, stands out clearly as the best as well as the simplest

In this country interest in respiratory function tests owes its origin to the work of van Slyke and his associates, particularly Binger They reported an accurate method of determining the total lung capacity without forced breathing and also vital capacity and its subdivisions His method, a modification of the dilution method invented by Davy (1800) and improved by Bohr (1907) and others, consists of rebreathing from an apparatus filled with a known mixture of hydrogen and oxygen After completely mixing the gases in the lung and apparatus, which requires about five minutes of quiet breathing, a determination of the dilution of the hydrogen in the apparatus permits an estimation of the total lung volume

$$\text{Vol } N_2 = H_2 \times \frac{\text{Vol } N_2 \text{ in sample}}{\text{Vol } H_2 \text{ in sample}}$$

$$\text{Lung Vol} = \frac{\text{Vol } N_2}{0\,791} \text{ since ordinary air contains 79 per cent } N_2$$

$$\text{or Lung Vol} = N_2 \times 1.264$$

When the vital capacity and its subdivisions, complemental air, tidal air and reserve air are also determined and then subtracted from the total lung volume there remains the residual air Binger later speaks of functional residual air (described by Lundsgaard and Schierbeck) as the amount of air contained in the lungs below the expiratory resting point They, like Bohr, stressed the necessity of comparing vital capacity with total capacity in evaluating changes in respiratory function since alterations in either one may occur with or without changes in the other and they pointed out the value of noting the midposition (axis of ventilation Goiffon)

The van Slyke-Binger method was not generally adopted possibly on account of the danger entailed in the use of an extremely inflammable hydrogen-oxygen mixture Working in the same institute and later at McGill University, Montreal, Christie developed a useful and safe modification of the van Slyke Binger technic In this method the closed system is filled with air and oxygen alone instead of an oxygen hydrogen mixture and the dilution of the nitrogen which is present in the lung at the beginning of the test is accomplished with oxygen The amount of oxygen utilized by the metabolism of the subject during the test is measured, subtracted from the total volume of the closed system at the beginning of the test and the mixture of nitrogen in the apparatus at the end of the test estimated by analyzing the percentage of oxygen which remains From these figures the total lung volume can be calculated

$$x = \frac{y\,(a-b)}{91-y} - d$$

x = Lung Vol in cubic centimeters.
y = Percentage of N_2 at end of experiment[1]
a = O at beginning in cc
b = O absorbed in cc
d = Dead space in the spirometer in cc

It is difficult to give adequate emphasis to Christie's work

[1] Correction is made to allow for N_2 excreted during the test while breathing an atmosphere of 41 per cent oxygen by subtracting 65 cc from the measured functional residual air and an additional 15 cc to allow for the difference in nitrogen tension in room air (79 per cent) and in the oxygen mixture (56 per cent)

since we are concerned in this paper only with its bearing on the vital capacity test He showed that although residual air and vital capacity each may vary from observation to observation as much as 300 cc , due to fortuitous changes in muscular effort, the functional residual air (reserve air plus residual air) is much more constant since its measurement depends on gas mixture rather than forced voluntary muscular effort With this method he studied the loss of elasticity of the lung in emphysema by measurements of intrapleural pressure taken simultaneously with graphic records of the total capacity and its subdivisions and he confirmed previous findings that the vital capacity is reduced and the residual air increased in emphysema He also found in emphysema the reserve air diminished and that when tested at the end of a test for vital capacity it is much less than when tested after quiet breathing

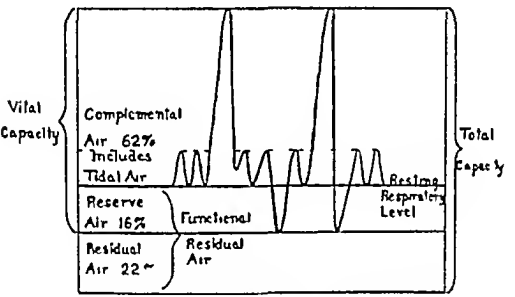
Using the Christie modification of the van Slyke-Binger method, Hurtado in McCann's clinic has made extensive ob servations on a group of 50 normal young men and 50 normal young women of an age averaging twenty-three years They found that whereas in different subjects the absolute volumes of the various divisions of the total lung volume show great individual variations, the proportional values expressed in terms of the total lung capacity of the individual give very constant results

Total capacity = 100 per cent	Vital capacity = 100 per cent
Vital capacity = 78 per cent	Complementary air = 80 per cent
Complementary air = 62 per cent	Reserve air = 20 per cent
Reserve air = 16 per cent	
Mid capacity = 38 per cent	
Residual air = 22 per cent	

They have also correlated their findings with all of the body measurements suggested by other workers and found best correlation with the body height They go further along these lines, however, and adopt a method devised by Thomas, whereby the volume of the lung fields on an x-ray plate is measured Excerpts of Hurtado and Fray's description of this

technic follow (omissions from their text are not here indicated)

"Radiographs of the chest were obtained at the end of maximum expiration, maximum inspiration, normal expiration and, in most instances, at the end of normal inspiration These four exposures were obtained on two films in the following manner One of the films was first exposed at the end of maximum expiration, and a second exposure was made on the same film at the end of maximum inspiration This film, when developed, shows the bony thorax and the diaphragm at both phases of respiration



The Lung Volume and its Subdivisions
(after Christie, volume percentages from Hurlado)

Fig 186

"It is of greatest importance that both exposures be made at the proper phase of respiration i e after maximal effort, since the data obtained are used for the prediction of normal pulmonary capacity

"The second film was obtained in a similar manner, varying only the phase of respiration for the exposures to normal expiration and normal inspiration

"The films were obtained in the recumbent prone position The target film distance was 6 feet

"Films obtained in this manner show the degree of expansion of the thorax and of the excursion of the diaphragm

during maximal and quiet respiration A planimeter which recorded areas accurately up to 900 sq cm was constructed

"With this instrument the areas of the lung field were determined from the films obtained at the end of maximum and of normal expiration and inspiration The tracer arm was moved along the following course The left axilla, left half of the diaphragm, right half of the diaphragm, right axilla, right apex and finally swept across the spine to the starting point at the left apex The difference in the area of the lung fields at maximum expiration and at maximum inspiration represents the increase in area during maximal respiratory effort Similarly, mensuration of the film taken at the end of normal expiration and inspiration yields data concerning the difference in area to be used in measuring reserve, complementary and tidal air, etc

"It was thought that a better approximate value of the size of the chest cavity could be obtained from combined external and radiological measurements We have multiplied in all cases the area of the lung fields (the area of the heart included) expressed in square centimeters, by the corresponding anteroposterior diameter (depth) of the chest measured externally in centimeters The result is designated in this paper as the 'radiological chest volume'

"In regard to the total capacity, we find that the highest correlation is obtained when the 'radiological chest volume' (at maximal inspiration) is used It is correlated significantly although in a lesser degree, with the area of lung fields (also at maximum inspiration) and with the body height

"The vital capacity is also better correlated with the 'radiological chest volume' Its correlation of $+0.7174 \pm 0.0467$ is the highest of the series, and consequently will be advantageously taken as the basis for the prediction of the normal pulmonary capacity in a given case It is interesting to observe the almost valueless correlation between the vital capacity and the body surface area, a rather surprising finding as it has been widely accepted in clinics, following the work of West in 1920

"It has now been shown that in the total series of correlations between the total pulmonary capacity and its components and the physical and radiological measurements, the highest and most significant correlation coefficient has been observed between the vital capacity and the 'radiological chest volume' This fact indicates that if the chest volume is known in a given case, the vital capacity may be predicted with a fair degree of accuracy by means of the regression formula derived from the correlation coefficient The regression formula is

$$\text{Vital capacity (in liters)} = (\text{radiological chest volume (in liters)} \times 0.24) + 1.22^{1}$$

Other fractions of the total capacity may be inferred from the percentage values which the vital capacity, the mid capacity, and the residual air usually constitute of the total volume (78, 30 and 22 per cent respectively)"

These studies by Hurtado *et al* provide figures for pulmonary capacity and its normal subdivisions in healthy male and female college students The wide variations in vital capacity and its subdivisions become much smaller when these volumes are expressed as a percentage of the patient's capacity Thus vital capacity maintains a mean value of 78 per cent of total capacity and complemental air 62 per cent Similar studies are in progress in various forms of pulmonary disease, some of which have been reported In emphysema they confirm the previous findings of others of changes in subdivisions of pulmonary capacity and reaffirm the need for examining the ratio of residual air to vital capacity and believe this figure presents a good index of respiratory disability Recently reported studies on pulmonary fibrosis lead them to attempt correlation between such measurements with others made during or after exercise

In summary we may evaluate vital capacity in the light of the facts enumerated in this paper which have emerged from some of the recent work on respiration In the first place, normal standards can best be obtained from standing height In the second place, very helpful information can be obtained by measuring x-ray films of the thorax and in normal young adults these measurements conform more closely with actual pulmonary capacity than do any other body measurements Thirdly, vital capacity when reduced by different types of lesions may owe its reduction to alterations in the various subdivisions of total lung volume and should, therefore, be studied in conjunction with residual air and total capacity This entails difficult technic, elaborate apparatus and laborious chemical analyses and even then the meaning of the exact results thus obtained is still to be determined

Simple and extremely valuable studies can be made, however, by determining vital capacity with a recording spirometer (such as the Benedict metabolism machine) with which tidal air, reserve air and complemental air are easily measured The figures obtained are then compared with Dreyer's normal tables for vital capacity based on standing height, and with the normal ratio of reserve air to complemental air worked out by Hurtado If any abnormality is noted, the vital capacity is further compared with calculated values of total capacity derived from x-ray films of the patient, by this means, information is made available for deducing all important changes in lung capacity Thus in heart failure, for example, the vital capacity and total lung volume are decreased while residual air is normal or decreased, whereas in emphysema the total lung volume remains normal and the decrease in vital capacity depends upon an increase in the residual air and a decrease in complemental air

Studies of this kind indicate whether the reduction in vital capacity arises from functional impairment of the chest wall or the lung or the circulation, and point the way to the development of accurate measurement of the severity of thoracic disease processes

BIBLIOGRAPHY

Hutchinson J Med Chir Trans., 39 137 1846
Dreyer G., and Burrell L S T Lancet, 1 1212 1920
Meyers J A Vital Capacity of the Lungs Baltimore, 1925
Peabody F W Arch Int Med., 16 846 1915
Peabody F W., and Sturgis C C *Ibid.*, 29 277 1922
Anthony A J Deutsches Arch f klin Med., 167 129 1930
Moncrieff A., Medical Research Council Special Report Series No 198 London 1934
van Slyke D D., and Binger C Jour Exp Med., 37 457 1923
Christie R V C Clin Invest., 11 1099 1932
Christie R V., and McIntosh C. A *Ibid* 13 2 9 1934
Hurtado A and Boller C Jour Clin Invest., 12 793 1933
Hurtado A., and Fray W W *Ibid* 12 807 1933
Hurtado A., and Fray W W *Ibid.*, 12 725 1933
Hurtado A., Fray W W., and McCann D W *Ibid.*, 12 833 1933
Hurtado A Fray W W., Kaltreder N L and Brooks, W., *Ibid.*, 13 169 1934
Hurtado A., Kaltreder N L., Fray W W., Brooks, W., and McCann D W *Ibid.*, 13 1027 1934
Hurtado A., and Kaltreder N L *Ibid.*, 13 1053 1934
McCann D W and Hurtado A Trans A Am Physicians 49 45 1934

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR. R W TE LINDE

THE JOHNS HOPKINS HOSPITAL

THE CLINICAL SIGNIFICANCE OF LEUKORRHEA AND ITS TREATMENT

THE term *leukorrhea* is applied to any vaginal discharge, exclusive of frank bleeding It is the most frequent of all gynecological symptoms and is estimated by various authors to be present in from 25 to 50 per cent of all women seeking the advice of a gynecologist Often the discharge causes little annoyance, but in women with highly sensitive nervous systems it may be extremely annoying and nerve racking It is a condition which may arise from any one of several lesions and frequently is the only symptom pointing to a pelvic disorder Upon hearing this complaint it becomes the duty of the physician to determine the underlying cause Quite often this is simple and the treatment is effective, leading to a prompt cure On the other hand, determination of the cause of the discharge may be extremely difficult and even gynecologist of wide experience encounters cases which try his diagnostic ability and tax his ingenuity in attempting to effect a cure The subject is not yet completely understood and certain phases of it are still worthy of research

Before dealing with abnormal vaginal discharge, it may be well to consider briefly the normal secretions found in the vaginal and vulval regions To do this requires some knowledge of the histology of the parts The labia majora contain sudoriferous and sebaceous glands and hence sweat and sebaceous material are found on the skin and mucosa covering them The labia minora are rich in sebaceous glands which produce a deposit of sebaceous material between the mucosal folds of

the labia and beneath the prepuce Bartholin's glands secrete a scanty mucus which is delivered into the vaginal vestibule The vaginal mucosa is devoid of glands The cervix, on the other hand, is rich in compound racemose glands that normally secrete a clear mucus which lubricates the vagina but is not sufficient in quantity to make the woman conscious of moisture in the vulval region This mucus is alkaline in reaction The content of the vagina is composed of this mucus together with desquamated squamous epithelial debris and a few leukocytes It is acid in secretion, owing to the activity of the vaginal flora, the chief organism of which is the large Gram-positive bacillus of Doderlein The epithelial débris of the vagina is usually most abundant in the upper part of the organ where it adheres to the wall in curdlike particles

Inasmuch as gonorrhea will be given separate consideration, it will be excluded from this discussion, after noting the important fact that gonorrheal cervicitis is one of the most frequent lesions responsible for vaginal discharge

In considering the pathologic lesions underlying leukorrhea let us start at the upper end of the mullerian tract *Adnexal disease* is seldom responsible for it Although in gonorrhea one often finds salpingitis associated with a vaginal discharge, it is the coexisting cervicitis which is responsible for the latter A hydrosalpinx which periodically empties through the uterus into the vagina has been described but such a lesion is so rare that it is of little practical importance A watery blood-stained discharge has also been reported as a symptom of that rare lesion, primary carcinoma of the tube

Contrary to earlier and erroneous opinions, the corpus uteri is seldom responsible for leukorrhea *Premenstrual hypertrophy* was once thought to be an inflammatory lesion and a frequent source of leukorrhea, but since the work of Hitschmann and Adler it has been recognized as part of the normal physiologic cycle It is, however, the secretory phase of the cycle and probably contributes to the slight mucoid discharge noted a few days before menstruation by so many women who are otherwise free from abnormal discharge *Retained pla-*

cental tissue following full term delivery or incomplete abortion with resulting endometritis may give rise to a purulent or watery discharge between the periods of bleeding The history of the case and the pelvic findings usually readily establish the diagnosis In such cases there is always some degree of infection and it should be emphasized that the indication for curetting is hemorrhage If there is simply a blood tinged discharge and the hemoglobin shows no serious reduction, non interference will usually result in a cure With each succeeding menstrual period a portion of the infected endometrium and retained products will be cast off and finally the symptoms will disappear entirely Another lesion of the corpus occasionally responsible for leukorrhea is a *pedunculated submucous fibroid* Although the chief symptom of this condition is usually hemorrhage, as the tumor comes down toward the vagina it becomes infected, and weeps a discharge composed of serum, pus and a variable amount of blood Such tumors can and should be removed vaginally If other fibroids are present and hysterectomy is subsequently necessary, considerable time should be allowed to elapse before the operation to permit healing of the infection in the uterine cavity

Occasionally a large *polyp* arising in the endometrium may grow down through the cervical canal, become infected and produce a purulent discharge We have on a few occasions seen such a polyp grow to unusually large proportions during pregnancy and be responsible for a profuse leukorrhea The histologic study of such a polyp shows it to be composed of infected decidua In the nonpregnant uterus the removal of such a polyp by twisting or snare is usually very simple, but in the pregnant state this must be done with the greatest of care in order not to disturb the pregnancy

Carcinoma of the endometrium usually first makes its presence known by bleeding, but at times a watery leukorrheal discharge may be present between the spells of bleeding and rarely may be the only symptom *A priori* it might seem that the possibility of this serious lesion being responsible for the leukorrhea might demand a diagnostic curettage in all cases

of leukorrhea As a matter of fact, in most cases the lesion responsible for the discharge is obvious on speculum examination In addition it should be recalled that carcinoma of the endometrium in a large proportion of the cases occurs after the menopause and is so frequently associated with postmenopausal bleeding that the indications for curettage are plain However, in dealing with a watery discharge after the menopause, even without gross bleeding, a curettage should be done unless the explanation of the symptom is obvious without it

In considering the lesions responsible for leukorrhea the *cervix* is of prime importance Age, virginity, and parity are all important in classifying these cervical lesions Before the onset of the menses a vaginal discharge seldom occurs except in gonorrheal vaginitis which is excluded from this discussion After the onset of the menses, in both virginal and nonvirginal women, a clear mucoid vaginal discharge may occur due to an excess of the normal secretion of the cervical glands A smear of this shows it to be composed chiefly of mucus with a few leukocytes and epithelial cells Speculum examination shows an albuminous-like secretion coming from the external os The cervix itself appears normal, there being no evidence of infection In some patients a zone of so-called "congenital erosion" may be seen about the external os but in others this is absent The proper explanation of it lies in the fact that the columnar epithelium of the cervical canal which usually terminates at the external os, not infrequently extends beyond, forming a zone about the os which appears red due to the fact that it is covered by the single layer of columnar epithelium instead of the usual stratified squamous type The treatment of this form of leukorrhea may be somewhat of a problem in young women Although the patient can usually keep herself comfortable with an occasional douche, one hesitates to institute the douching habit at such an early age Local applications of antiseptics are not logical as there is no infection and clinically they do little good The destruction of part of the cervical glands by radial strokes of the cautery or by electrical coagulation usually gives satisfactory results

Young virginal women are seldom troubled with a *muco purulent leukorrhea* but in the sexually active *nongonorrheal endocervicitis* is not uncommonly productive of such a discharge In this type of cervicitis the speculum examination may show some reddening of the vaginal portion of the cervix but often the chronic inflammation is entirely limited to the endocervix while outwardly the cervix may be quite normal The mucopurulent discharge may grossly show no difference from that produced by the gonococcus Inasmuch as the latter organism can usually not be found in smears after a month or more following inception of the infection, a negative smear by no means excludes gonorrhea Other stigmata of gonorrhea should be looked for and the sexual partner investigated Frequently the diagnosis will depend upon the data obtained by examination of the male Gonorrhea having been ruled out, the matter of treatment has to be decided upon Weekly or biweekly applications to the endocervix with swabs saturated in 10–20 per cent silver nitrate or mercurochrome of the same strength may be of value Often one sees improvement under this treatment but all too often there is an early recurrence Increasing experience teaches us that destruction of the infected cervical glands with the actual cautery blade or electrocoagulation usually brings about a permanent cure

Coming now to the *parous cervix* as a source of leukorrhea, we are dealing with a structure quite changed from that of the nulliparous state Every cervix which has been dilated by childbirth and most of those instrumentally or naturally dilated as the result of an abortion show some lacerations In the milder degrees of laceration the cervix may upon healing return practically to its nulliparous state Frequently, however, the healing of the lacerations with contractions due to scar tissue causes an eversion of the endocervix and the external os is seen to be gaping widely At the time of the laceration some infection always gains access into the cervical tissues This infection may heal spontaneously in a very short time but unfortunately it may persist and its presence in the region of the cervical glands may stimulate an excessive cer-

tion of mucus and pus In such cases the leukorrhea may date from childbirth or abortion but such need not be the case An everted cervix throws open the cervical canal widely to the vaginal flora and the single layer of endocervical epithelium does not afford adequate protection against the organism Thus at any time after the laceration the cervical tissue may be invaded and the leukorrhea appear months or years after the initial injury The mucopurulent discharge due to this type of cervicitis is characteristically thick and mucilaginous and often very profuse Fortunately it is not usually irritating to the skin of the vulva On speculum examination these lacerated cervices may show areas suggestive of early malignancy Biopsy and microscopical study of these areas should not be neglected Usually the microscopical picture is decisive but occasionally there are proliferative inflammatory changes which under low-power magnification suggest cancer Critical examination under the high power, however, will usually settle the matter There is a tendency to consider these lesions precancerous and, on this basis, to resort to radical surgery It should not be lost sight of that no one has ever traced a transition between these microscopical pictures of "cancer-like" lesions and true cancer

In considering the indications for treating the nonspecifically infected parous cervix, the subject may be viewed from several angles The discomfort and inconvenience caused by the leukorrhea is the reason for consultation in most instances, and the correction of these complaints in themselves is sufficient to justify treatment Not infrequently such a cervix is discovered in a routine physical examination during a search for a focus of infection in conditions supposedly due to chronic infection What can we promise the arthritic in whom such a nonspecifically infected cervix is found as to the effect upon her arthritis of removal of such a source of infection? We cannot honestly promise her anything and yet in this distressing disease most internists are agreed that every possible focus should be eradicated Although it is unlikely that the cervix is a focus from which organisms are entering the blood stream

and through it are transported to the joints, it is true that the elimination of infection from a cervix often causes a marked improvement in the general health and aids the patient in combating her arthritis The occasional improvement observed would seem to justify the eradication of the infection under such circumstances

What justification have we for treating the lacerated infected cervix as a prophylactic measure against future cancer? Although no one has ever been able to trace a transition histologically between chronic inflammatory changes in the cervix and carcinoma, there is some clinical evidence to show that such cervices are predisposed to malignancy The rarity of carcinoma of the cervix in nulliparous women has long been noted Pemberton and Smith in 1408 cases of chronic cervicitis which had been successfully treated with the cautery failed to find any patient who subsequently developed carcinoma These results would seem to indicate that from the standpoint of prophylaxis against cancer alone the treatment of chronic cervicitis is justified

Occasionally a woman who had had one or more children and desires a further pregnancy consults her physician who finds the pelvic organs normal except for a cervicitis of this type A mucopurulent plug in the cervical canal may act as an effective barrier against the ascent of the sperm and the clearing up of such a discharge may be all that is necessary to permit pregnancy

Having decided that a clearing up of the discharge is desirable for one or more of these indications how is this type of cervicitis best treated? Obviously a method is desirable which is most certain to eliminate the infection which incapacitates the patient for a minimum of time, and which leaves the cervix in the most normal condition for its function in menstruation and childbearing In our own experience with this type of cervicitis local applications and douches are little more than palliative measures and not much can be hoped for in the way of a permanent cure A consideration of the microscopical pathology of the infected cervix makes the reason

for this apparent The racemose glands of the cervix often reach to a depth of a centimeter into the fibrous stroma About these glands and nabothian follicles there is an infiltration of inflammatory cells far too deep for any surface antiseptic to reach The radical surgical procedure of amputation suggests itself The generally accepted disadvantage of this procedure is that the shortened cervix fails in the later months of pregnancy, and premature labors and miscarriages are frequent Then, too, a surgical amputation is a major operation requiring a long period of hospitalization and not without real danger of postoperative hemorrhage This complication is apt to take place from ten to twelve days after operation when the catgut disintegrates These considerations practically limit the indications for amputation to cases in which future childbearing is not a consideration and in which the amputation is only part of some surgical procedure which calls for long hospitalization Trachelorrhaphy carries with it also the possibility of postoperative hemorrhage and usually removes only part of the diseased glands All too often it simply inverts the diseased endocervix, thus hiding it from view but not removing the source of the discharge The surgical removal of a cone of the endocervix and relining of the canal with a flap of mucosa from the vaginal portion of the cervix was described several years ago by Sturmdorf and has enjoyed some popularity We have occasionally used it when the patient was to be hospitalized for other operative procedure but since equally good results can usually be obtained by a lesser procedure we have used it with decreasing frequency

Cauterization of the cervix with the actual cautery blade, as described by Hunner, has been used these many years with increasing popularity It may be done either with or without general anesthesia The period of incapacity of the patient is almost *nil* If properly done, it does not interfere with future childbearing, and as a means of eradicating the leukorrhea it is most effective A second cauterization may occasionally be necessary especially if the first has been done without anesthesia, but the ultimate result is satisfactory in a very large

percentage of cases Greatly lacerated everted cervices, rid dled with nabothlan cysts, which formerly were amputated, will yield to this treatment successfully and it restores the cervix to a surprisingly normal appearance

Radial cauterization may usually be done as an office pro cedure without nnesthesia with surprisingly little discomfort to the patient. Occasionally a nervous woman will require the use of nitrous oxide Some of the unanesthetized women insist that there is no discomfort associated with the procedure but many complain of a cramplike pain in the midabdomen This, however, is of short duration and usually preferable to the discomfort of an anesthetic The canal is cauterized in a radial manner with a slender cautery blade leaving uncauter lzed areas between the strokes When there is eversion the everted lips are cauterized with linear strokes and the cystic follicles destroyed individually by momentarily plunging the cautery blade into them Many gynecologists carry out this procedure by electrocoagulation instead of the actual cautery We have had no personal experience with it but see no objec tion to this procedure The actual cautery has given such good results that we have been loath to forsake it for any other method Within a few days following cauterization a profuse and often rather foul smelling discharge begins and persists usually for about two or three weeks until the slough ing is complete During the latter part of this period the dis charge is apt to be tinged with blood Rarely profuse bleed ing occurs necessitating packing Following the period of sloughing, healing, takes place and with it there is a gradual cessation of discharge During this period of sloughing and healing daily douches are required for the patient s comfort Potassium permanganate solution, 1 5000, is quite satisfactory but the following douche, used to the quart, is less objection able to most patients Boric acid, 4 ounces nium, 1 ounce, carbolic acid, 2 drachms, oil of peppermint, 2 drachms At the end of five to six weeks the discharge has usually largely disappeared but the last trace may persist for some time If there is a partial persistence of the leukorrhea one should not

be too anxious to cauterize a second time, for in our experience often improvement goes on for several weeks and even months following cauterization While healing is progressing, the patency of the cervical canal should be tested and, if necessary, it should be dilated from time to time A failure to observe this precaution may result in an incomplete or even complete stenosis This may cause a persistence of the discharge due to inadequate drainage of the cervical canal and to dysmenorrhea or even complete retention of the menstrual blood

Another somewhat common lesion responsible for leukorrhea is the *cervical polyp* Polyps may arise from the external portion of the cervix or from the cervical canal They are almost invariably infected and, since they contain glands, usually pour forth a mucopurulent discharge Often the discharge is blood-tinged and frank bleeding may occur after coitus, defecation, or douching The diagnosis is made on speculum examination Occasionally the external os may require dilatation before the polyp can be brought into view These small growths can usually be twisted off with a clamp in office or dispensary Such a removal may, however, be incomplete and a gas anesthesia may be necessary for dilatation of the canal for curettage of the base The application of the cautery to the base of the pedicle is often useful Every polyp removed should be sectioned for microscopical study Although polyps rarely become malignant and carcinoma of the cervix rarely originates as a polyp, the occasional case of malignancy discovered well repays for the trouble of this routine

Aside from *cervical stenosis* due to cauterization this condition may occasionally result from other operative procedures After the menopause a certain amount of cervical narrowing occurs normally, but at times, as the result of adhesions between the opposing surfaces of the cervical canal, the occlusion may be complete This postmenopausal stenosis may exist without symptoms but infection retained behind the closed cervix may cause a pyometra The stenosis resulting from carcinoma of the cervix particularly that following radia-

tion is especially apt to give rise to pyometra since the cervical growth supplies the necessary infection The retained pus often intermittently breaks through the cervical adhesion and gives rise to a purulent and often blood tinged discharge Cervical dilatation is all that is usually required to clear up the discharge

The *vagina* is the source of leukorrhea much less frequently than the cervix The mucosa being covered by many stratified layers of epithelium is much more resistant to infection than the endocervix *After the menopause* the vaginal mucosa becomes smoother and the epithelial lining considerably thinner This change apparently makes it much more vulnerable to infection and hence vaginitis after the menopause is not uncommon Aside from the age factor nothing specific regarding its etiology is known In senile vaginitis the smooth mucosa is diffusely reddened and often shows small punctate areas of ulceration The discharge is milky or yellowish in color but often streaked with blood At times adhesions may form between the apposing surfaces and the rupture may give rise to frank hemorrhage The discharge is frequently markedly acid and this reaction suggests the treatment with soda bicarbonate douches which are often attended with some success The application of 10 per cent silver nitrate directly to the vaginal mucosa twice weekly, together with daily cleansing douches is often beneficial and sometimes curative

In 1837 Donne described a flagellated parasite in vaginal secretion which he called *Trichomonas vaginalis* Its presence has been generally recognized since that time and it was thought to be a harmless vaginal parasite occurring in a fair percentage of women especially during pregnancy It has been found, however in girls before puberty and in women after the menopause In 1916 Hoehne first described a form of vaginitis associated with Trichomonas infection which he felt was the direct result of this parasite Since then many gynecologists have reported long series of such cases and most of them are agreed that the protozoon is responsible for the

disease The mucosa of the vagina and vulva are diffusely reddened and the patient complains of a great deal of vulval irritation Often the upper vagina and cervix have a peculiar red stippled appearance The discharge, which may be profuse or scanty, is milky white or slightly yellowish and frequently frothy in consistence The diagnosis is established by finding the parasites in a hanging drop of the vaginal discharge mixed with physiologic saline

In spite of this rather characteristic clinical picture associated with these organisms there is still some doubt on the part of good observers as to the etiologic relationship Certain observers have concluded that the bacterial flora, especially streptococci, often found with the Trichomonas, are the *real inciting agents in the vaginitis* The weak points *in the* chain of evidence incriminating the Trichomonas as the primary cause are as follows The organism is frequently found in women without any evidence of vaginitis A very similar vaginitis is occasionally seen from which the Trichomonas cannot be recovered No one has ever been able to produce the disease by inoculation of the normal vagina with a culture of the flagellate

In spite of these objections, however, the fact remains that these organisms are usually associated with a fairly distinctive clinical entity, and as the vaginitis improves under treatment the organism disappears, whereas with recurrences there is a reappearance of the Trichomonas

The source of the infection is not known Fecal contamination caused by wiping fecal matter forward has been suggested but most protozoologists believe that Trichomonas vaginalis and Trichomonas intestinalis are not identical Urologists have recently demonstrated Trichomonas infection in the prostate and have suggested this as a source of infection in the female Davis believes that most of the evidence at present points to bathing as the most likely source of infection He bases his view largely on the higher incidence of the infection during the summer months when fresh water lake bathing is prevalent

The methods suggested for the treatment of Trichomonas vaginalis vaginitis are manifold Within the past five years almost every gynecologist reporting cases in the literature has suggested his own method of treatment Although the results are for the most part fairly satisfactory, often weeks and months of treatment are necessary and frequent recurrences on cessation of treatment are not uncommon Several of the procedures used are enumerated but this list is by no means complete

J P Greenhill Vagina scrubbing with green soap, application of hexylresorcinol, glycerin tampon, douching with 5 per cent lactic acid

C H Davis Vaginal scrubbing with green soap, application of one of the several following chemicals (1) Five per cent mercurochrome, (2) 1 1000 hexylresorcinol, (3) quarter strength Lugol's solution (4) 1 per cent aqueous gentian violet solution, (5) 1 1000 merthiolate This is followed by an ichthyol glycerin or glycerin tampon and daily douches of mercuric chloride, 1 5000

Hoehne, Schmidt and Kamniker Washing the vagina with mercuric chloride, 1 1000, followed by 10 per cent borax glycerin solution application

Holden and Kleegman Application of full strength pyroligneous acid followed by tampons of Lassar's paste.

Goodall Daily suppository of

Picric acid	1.2 grains
Borogkeride with gelatin	100.0 grains
Sodium teraborate	5.0 grains
Zinc borate	0.5 grains
Hydrastine	5.0 grains

Daily douches of lactic acid solution 0 5 per cent

Innumerable other methods of treatment may be found in the literature We have had our best results with scrubbing the vagina twice weekly with green soap supplemented by the daily use of a picric acid suppository at bedtime These may be purchased under the trade name of Wampole's picric acid cones The following morning any cleansing douche is used

Within the past few years a good deal of literature has appeared indicating that *yeasts* may be the primary causative agents in certain cases of vaginitis and vulvitis Castellani found that Monilias are absent from the normal vaginal flora but present in certain cases of vaginitis Further observations by Castellani and Taylor, Cron, Plass and Davis show that yeast infections are not uncommon in the vagina The fungus may be found in fresh preparations of the vaginal secretion diluted with salt solution These organisms are more frequently present during pregnancy and Plass had produced thrush experimentally by inoculation of infants' mouths with the Monilia obtained from vaginal secretions, indicating the possibility of transmission from mother to child at birth There is much doubt, however, among many good observers whether vaginal Monilias are ever responsible for the vaginitis, and the disease has never been produced experimentally by vagina inoculation We have seen a single case during pregnancy in which a very much inflamed vaginal wall was covered with a whitish curdlike substance rich in yeast A 1 per cent aqueous solution of gentian violet is considered the treatment of choice but our single case failed to respond to any treatment before delivery after which the condition subsided spontaneously Davis also recommends douches of bichloride of mercury, 1 5000, and the application of 5 to 10 per cent mercurochrome to the vagina

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DR PAUL W CLOUGH

THE JOHNS HOPKINS HOSPITAL

THE TREATMENT OF FUSOSPIROCHETAL INFECTIONS (VINCENT'S DISEASE)

By fusospirochetal infection is understood any infection caused by the spirochetes and fusiform bacilli described by Vincent in the ulcerative pharyngitis which is still commonly called Vincent's angina His findings have been confirmed amply by subsequent observers The spirochete (Borrelia vincenti) is a long slender organism showing one or several shallow undulations It stains faintly with the ordinary bacterial stains, such as Loeffler's methylene blue or dilute carbol fuchsin, and better with Fontana's silver nitrate method It can be seen easily in fresh preparations by darkfield illumination, and is actively motile It is an obligate anaerobe and can be cultivated only with great difficulty even in special spirochetal media

The fusiform bacillus (Fusiformis dentium) is a coarse, plump rod with pointed ends Large and small forms occur It is gram negative, but stains well with ordinary stains, and often shows some beading It is also an obligate anaerobe, but can be grown without great difficulty on suitable media Practically, however, diagnosis depends on demonstrating directly both organisms in properly prepared stained films from the ulcers The exact relation of these two organisms to one another is not definitely settled Some observers regard them as different morphological types of a single species, because they believe they can demonstrate in cultures transformation of one type into the other

As a rule these organisms have a relatively low virulence and show little power to invade the deeper tissues The initial

lesion appears most frequently on the gums, particularly about the lower molar teeth, causing at first tenderness, injection, and slight swelling of the gingivae, which bleed easily Shortly there appear along the gum margin small grayish or whitish areas of exudate, composed of the necrotic superficial layers of the mucous membrane and masses of bacteria If this membrane is pulled away it leaves an ulcer with an inflamed, ragged base, and a margin of deeply injected mucous membrane The margins are irregular in outline and ill-defined, never indurated or excavated The ulcers extend laterally and may coalesce There is a characteristic sickening, foul, slightly sweetish odor to the breath

In sections through such an ulcer three fairly distinct layers can be made out

1 A superficial necrotic layer consisting of cellular detritus, masses of mouth bacteria, and varying numbers of spirochetes and fusiform bacilli

2 An intermediate layer of acutely inflamed tissue in which the fusiform bacilli predominate

3 A deep layer containing masses of spirochetes, which appear to be the actively invasive agents

Throughout the lesion there are often streptococci in varying numbers There is little or no leukocytic infiltration of the tissues

The primary lesion may be on the tonsil (Vincent's angina), or on the gums (Vincent's stomatitis, trench mouth) From either location secondary lesions often appear on the mucous membrane of the lips, cheeks, tongue, palate or pharynx, and in rare instances practically the entire buccal mucous membrane may be involved Whenever the tonsillar region is affected the glands at the angle of the jaw are much enlarged With a gingivitis of the mandible the submentals and submaxillaries are more or less enlarged

In most cases the ulcers remain limited to a relatively restricted area The temperature is normal or only slightly elevated, and there is little or no constitutional disturbance The disease runs a self-limited course, and recovery occurs in

a few days The ulcers heal without appreciable scarring In uncomplicated cases there is no increase in the granular leukocytes In a few cases a marked lymphocytosis occurs

Occasionally, especially when a more extensive area is involved, there is fever with a temperature of 102° or 103° F, and a marked constitutional reaction More rarely, necrosis may penetrate into the deeper tissues, destroying the gums and exposing the roots of the teeth, which may loosen It may involve the underlying bone, causing an osteomyelitis Ulcerations in the throat may also penetrate very deeply, destroying the palate or the tissues at the base of the tongue, or the larynx, or it may perforate the lateral wall of the mouth or throat and produce a fistula In extreme cases a large part of the face may be destroyed The process may, in rare instances, involve practically any of the other mucous membranes It may invade the nasal passages, the middle ear, or the paranasal sinuses, causing a putrid discharge If the ethmoids or sphenoids are involved, there may be necrosis of the cranial bones, extension through the meninges, and development of a brain abscess It may extend into the pharynx, trachea and bronchi and, rarely, may arise primarily in the larynx without visible lesions in the mouth or pharynx The process may extend from the pharynx into the esophagus It may also involve the rectum and the colon, causing a foul, bloody diarrhea In which the organisms have been demonstrated Death has occurred from peritonitis following perforation of an intestinal ulcer The organisms have been demonstrated in some cases of gangrenous appendicitis The external genitals may be the site of fusospirochetal ulcerations They may constitute the primary infection, or the infection may be superimposed on syphilitic, chancroidal or other lesions, and give rise to deep phagedenic ulcers with extensive destruction of tissue The process may extend into the vagina and uterus

Postoperative or other skin wounds may become infected Hospital gangrene, and many cases of tropical ulcer fall into this category Gangrene of the finger or hand has been re

from outside sources must be the explanation of the epidemics of Vincent's infection, such as were observed in the armies during the World War Other epidemics have been described by a number of observers under peace conditions, both in institutions and in communities The direct communicability of the disease under these special conditions has been amply demonstrated It is therefore important that adequate isolation be carried out during the active infection, particularly during epidemic periods It is desirable to continue this for a reasonable period in convalescence if the organisms in the mouth are numerous However, to attempt to continue isolation until the mouth is entirely free from organisms is a practical impossibility, since in many cases they never disappear

Diagnosis—Diagnosis can almost always be made easily by demonstrating the presence of large numbers of both of the organisms in stained films from the exudate The presence of a few organisms only is not of diagnostic significance

Some care in making the preparations is essential Films made by rubbing over the surface of the exudate may fail to show the organisms Material should be obtained from the depths of the ulcer under the membrane, and from the margins of the lesion where the anaerobes are numerous If no spirochetes are demonstrated by the usual stains, films should be stained by Fontana's silver method, or perfectly fresh, warm material should be examined by dark field illumination This is particularly important in the case of sputum Spirochetes disintegrate rapidly in sputum or pus outside the body, and examination of material that has stood for more than an hour is generally useless

The possibility of Vincent's infection should be thought of in every ulcerative condition of the mouth and throat, in every case of postoperative pneumonia, lung abscess, or bronchiectasis, and in all putrid or gangrenous processes, whether in the nose, ear, respiratory tract, or on the genitals, or skin

Diagnosis is not completed by the demonstration of the organisms An acute Vincent's infection does not exclude the

presence of some underlying organic disease, whether it be a carcinoma of the tongue, an acute leukemia, or an agranulocytic angina Furthermore, Vincent's infection may be associated with other acute infections of the mouth and throat, particularly with diphtheria In all suspicious cases cultures must also be made to exclude diphtheria

Treatment—The methods in general use may be classified as follows

1 Local mechanical cleansing measures

2 Pastes, irrigations, or mouth washes containing oxidizing agents

3 Local applications of general antiseptics

4 Local and systemic application of specific spirocheticidal drugs

There can be no doubt as to the importance of good oral hygiene in the prevention of Vincent's stomatitis The teeth should be kept clean and free from tartar, and pyorrheal pockets should be cleaned out mechanically by suitable dental measures If the pockets are extensive and deep, extraction will often be advisable, particularly in patients with persistent or recurring stomatitis Such areas, when neglected, have aptly been described as anaerobic incubators, and, by harboring large numbers of fusospirochetal organisms, constitute a constant menace to the patient

During an acute attack the ulcers should be kept as clean as possible by gentle swabbing, or irrigation with fluids, preferably under pressure Removal of the accumulated sordes is doubtless helpful in itself, and is a necessary preliminary to the effective use of local applications The nature of the irrigating fluid is a matter of relative indifference, provided it is not irritating Among those most used may be mentioned 2 per cent green soap solution, half strength hydrogen peroxide, and 2 per cent sodium perborate The oxygen liberated by the latter doubtless helps mechanically in the cleansing process

Tooth extraction, if not imperative, should be postponed

since serious complications have followed extraction done during the acute stage of the disease

Local applications are relied on chiefly in the treatment of stomatitis and pharyngitis They should be noncaustic, nonirritating and nontoxic, they should penetrate deeply into the affected tissues, and maintain their activity for some time after absorption, and they should exert a specific destructive action on at least one of the organisms Most of the agents in use are deficient in one or more of these respects

The use of oxidizing agents is based logically on the fact that the fusospirochetal organisms are strict anaerobes, and the liberation of nascent oxygen should make conditions highly unfavorable for their growth However, these agents are rapidly reduced when they come into contact with the tissues, and they have little or no penetrating power, so that they cannot reach the organisms in the deeper layers of the tissues Nevertheless, they appear to exert a definite beneficial effect in most cases of stomatitis or pharyngitis

Among the substances most widely used are

1 Chromic acid, in 5 to 7 per cent solution, painted on the lesions once daily

2 Copper sulphate, in powdered form, or as a 10 to 50 per cent solution, or as a mouth wash in 2 per cent solution

3 Potassium permanganate in 1 100 to 1 2500 solution This stains the teeth to some extent

4 Potassium chlorate in 4 per cent to a saturated solution, as an irrigation and mouth wash, or painted over the ulcers in saturated solution It has also been used extensively as lozenges in dose of 2 to even 4 Gm daily, but it is not without danger in such doses, when swallowed

5 Sodium perborate, applied as a paste, has come into more general use since its successful application in the army during the War To be effective the procedure must be carried out thoroughly Liberal quantities of a thick paste are spread with the fingers over the gum margins of all the teeth, inside and outside With a toothpick it is worked gently into the spaces between the teeth, and into any pockets which may

ase of Vincent's angina cured in four
on It is still impossible to draw
a degree of its effectiveness
the usual simultaneous
it, which alone are
the results on the
nerous individual cases
promptly and favorably
ne after the usual local
nd the disease appeared to
Any one who has treated
have had similar experiences
ppears to be shortened Thus,
one fourth the time required"
was employed Harris,[1] in a large
ina treated by intravenous injections
eported healing in forty-eight hours,
ions (one fatal) Relapses were re-
lose, but none were observed in patients
injections at one week intervals Lesions

tion in glycerin or glucose solution may be painted over the lesions once daily (at first even two or three times daily) It must be worked well into all the crevices and pockets It is distinctly painful 'It should not be rinsed out, and may be swallowed without injury I have found no reports of arsenic poisoning following such use Rapid recovery has followed in a large majority of the cases Neoarsphenamine and stovarsol (spirocid) have also been used in the same manner with similar results

In most cases local applications of sodium perborate or other oxidizing agents have alternated with applications of arsphenamine, and it is impossible to determine the relative part played by the two substances in bringing about recovery As far as can be judged from American experience, their combined use appears to be the best routine method of treatment now available

Shortly after the spirocheticidal action of bismuth preparations had been demonstrated by their curative action in experimental rabbit syphilis, their use as local applications was tried in Vincent's infection During the past ten years they have come into extensive use, particularly in France and in South America Mangebeira-Albernay was among the first to use them and is an enthusiastic advocate [1] He pointed out that bismuth preparations are less toxic, and less irritating and painful than any other preparations in use, and that they are more effective in softening and breaking up the necrotic membrane He advocates the use of acid potassium bismuth tartrate in 10 per cent solution in water or glycerin, or as a 30 per cent ointment, painted or smeared over the lesions once daily Even the severe cases required only three applications The results reported were fully as good as those obtained here with other methods of treatment

The administration of arsphenamine preparations by intravenous or intramuscular injection is generally regarded as the most effective method of treatment of fusospirochetal infections They have been used extensively since Ehrlich in

[1] Laryngoscope, *1929, 39, 1*

1910 first reported a case of Vincent's angina cured in four days by one dose of salvarsan It is still impossible to draw final conclusions as to the precise degree of its effectiveness in stomatitis and angina, because of the usual simultaneous employment of local measures of treatment, which alone are usually effective With this reservation, the results on the whole appear distinctly favorable Numerous individual cases have been reported which responded promptly and favorably to the administration of arsphenamine after the usual local measures of treatment had failed, and the disease appeared to be running an unfavorable course Any one who has treated many cases of the disease will have had similar experiences The duration of the disease appears to be shortened Thus, Albray reported healing "in one fourth the time required" when local treatment only was employed Harris,[1] in a large epidemic of Vincent's angina treated by intravenous injections of sulpharsphenamine, reported healing in forty-eight hours, with but three exceptions (one fatal) Relapses were frequent after a single dose, but none were observed in patients who received three injections at one week intervals Lesions about the gums were notably slower in healing than those in the pharynx

Faber, and Barenberg and Bloomberg have reported similarly good results following the administration of neoarsphenamine, or sulpharsphenamine intramuscularly in children, even without any local treatment They noted no striking local improvement until the third or fourth day They found healing somewhat more rapid in those children in whom local applications could effectively be made Favorable results have also been reported after use of bismarsen intramuscularly (Kolmer) and after oral administration of stovarsol (Hutter, etc.)

The effectiveness of arsphenamine can be demonstrated more convincingly in the severer forms of this infection, particularly in bronchial and pulmonary fusospirochetosis The normally high mortality, and the impracticability of local treatment eliminate sources of confusion present in the evaluation

[1] New York State J Med 1913 3 136

of the results of treatment in buccal infections The work of numerous observers has shown that, after arsphenamine administration in cases of pulmonary abscess and gangrene, the mortality is markedly reduced, and complete recovery is usually obtained provided the treatment is started early The spirochetes disappear quickly from the sputum, and the latter loses its characteristic infectiveness for animals In the later stages of the disease less benefit has been obtained, though even then the sputum may be diminished, it may lose its foul odor, and the general health may be improved Much of this work is summarized in the monograph of D T Smith [1]

More recent work has demonstrated the effectiveness and greater safety of relatively small doses of neoarsphenamine, particularly in patients who are critically ill In such cases initial doses of 0 05 to 0 1 Gm seem advisable Injections may be given at three-day intervals at first, later once a week If well borne, the dose may be increased gradually, but 0 3 Gm seems to be the maximum needed

Favorable results with arsphenamine have been reported in other types of fusospirochetal infection Thus, in cases of gangrene of the hand, prompt cure has followed a single dose of arsphenamine, though as might be expected, the local application of antiseptics and oxidizing agents was quite ineffective Recovery has also been reported in isolated cases of involvement of the colon following arsphenamine by mouth and intravenously

The arsphenamines are not invariably effective Numerous individual cases have been reported with a fatal outcome despite its administration In some of these cases arsphenamine was not given until late in the disease, but in others it was given early While in some cases death may be attributed to an unfortunate "accident," such as the erosion of a large vessel, or development of a brain abscess, in others it must be regarded as due directly to the intoxication from the spirochetosis itself, or to streptococci and other associated organisms Furthermore, a considerable number of cases has been

[1] Oral Spirochetes and Related Organisms, Williams & Wilkins, 1932

reported of individuals who developed an acute spirochetosis, sometimes severe, while receiving a course of arsphenamine injections for syphilis This observation has aroused some scepticism as to the effectiveness of arsphenamine in this infection Such an attitude seems quite unwarranted A simple and probable explanation may be found in the assumption that the spirochetes have become "arsenic fast in the sense of Ehrlich Such an arsenic fast state is well recognized and amply demonstrated in the case of some other forms of spirochetal and spirillar infection, and it is reasonable to expect that a similar resistance to arsenic might develop in the case of this species

Reactions to arsphenamine injections occur in patients with Vincent's angina, as might be expected They are of the same types and occur with about the same frequency as in patients with syphilis A few deaths have been reported This risk, while slight, raises serious doubt as to the advisability of employing arsphenamine injections as a routine procedure in simple spirochetal infections of the mouth and throat However, it should be given promptly in the more serious types of the disease, or in cases with lesions which are inaccessible to local applications and without much delay, in patients with local lesions which are advancing despite other methods of treatment

Neoarsphenamine (in small doses) appears to be the best preparation to use Sulpharsphenamine, because of its greater toxicity, is the least desirable except perhaps for patients with whom intravenous injection is impracticable

In case patients with severe infection do not respond to arsphenamine one may try intramuscular injections of bismuth (e g 2 cc of 1 5 per cent solution of bismuth and sodium tartrate) as in the treatment of syphilis There is as yet relatively little evidence to prove the degree of its effectiveness It has been given without effect (usually along with arsphenamine) in some of the fatal cases

Antimony might also be tried Driscoll[1] reported prompt

[1] Virginia M Monthly 1914 41 11

cures of two cases of Vincent's angina following daily intravenous injections of 5 cc of a 1 per cent solution of antimony and potassium tartrate (three or four doses in all) One was an arsenic-fast case

In conclusion, it is evident from the multiplicity of methods of treatment in use that no one is altogether satisfactory Every method thus far employed has occasional failures In cases in which any one method of treatment has failed, recovery may follow a change to some other method which in general is no better than the one it replaces Interpretation of results is made difficult by the great variability in the severity of the infection, and by the fact that most cases of simple mouth and throat infection recover within a relatively short time, regardless of the treatment There are no large series of cases reported in which any single method has been tested under adequately controlled conditions The results reported largely represent the personal impression of the observer, based in the main on experience with a single scheme of treatment Such conclusions can be accepted only with reservation

In summary, the following scheme is suggested

1 Adequate but gentle local cleansing measures, including the frequent use of dilute oxidizing mouth washes

2 Daily applications of oxidizing agents, of which sodium perborate seems to be the best, followed by an application of arsphenamine, as a paste, or acid potassium bismuth tartrate in 10 per cent solution, or 30 per cent ointment

3 In severe, spreading, or resistant cases, small doses of neoarsphenamine intravenously, or in small children, sulpharsphenamine intramuscularly

4 In cases of pulmonary lesions or other infections inaccessible to local applications, neoarsphenamine intravenously as soon as the diagnosis is made

5 In infections which do not respond to these measures or which appear to have become resistant to arsenic, intramuscular injections of bismuth, or others of the alternative procedures discussed

Medical Clinics of North America
May 1935 Baltimore Number

CLINIC OF DRS SYDNEY R MILLER AND WALTER C MERKEL

UNION MEMORIAL HOSPITAL

PULMONARY ACTINOMYCOSIS

ALTHOUGH actinomycotic infections in man have been well recognized, particularly since the work of Wolff and Israel in 1891, there still remains a number of unanswered problems in the etiology, diagnosis and treatment of such infections particularly when they involve the lungs For this reason it would seem appropriate to report the following case

On September 22, 1934, a white male, aged thirty four, from Texas, entered the hospital complaining of pain in his left upper chest, dyspnea, fever, cough and blood tinged expectoration

Previous History—This man's previous health history had been singularly good As a matter of fact he had had no occasion to consult a physician for a number of years, except for the most minor type of ailment He had undergone no surgical operations except the removal of his tonsils and adenoids years ago He had had a great deal of dental trouble resulting in considerable bridge work but had not required any dental treatments for some time prior to the onset of his present illness His business, that of a wholesale grocer did not bring him into any contact with cattle horses barns or stables His habits were exemplary with the possible exception that he led somewhat too sedentary an existence and was a bit overweight for his height though muscularly well developed He was married and had two healthy children

Present Illness—Approximately two months prior to coming here he was taken one morning while walking to his

business, with pain in his left upper chest and in the region of his heart Though the pain itself was not agonizing, the fact that it radiated to his shoulder and down his left arm rather frightened him, and he feared that he might have some serious heart affection He promptly consulted his physician, who,

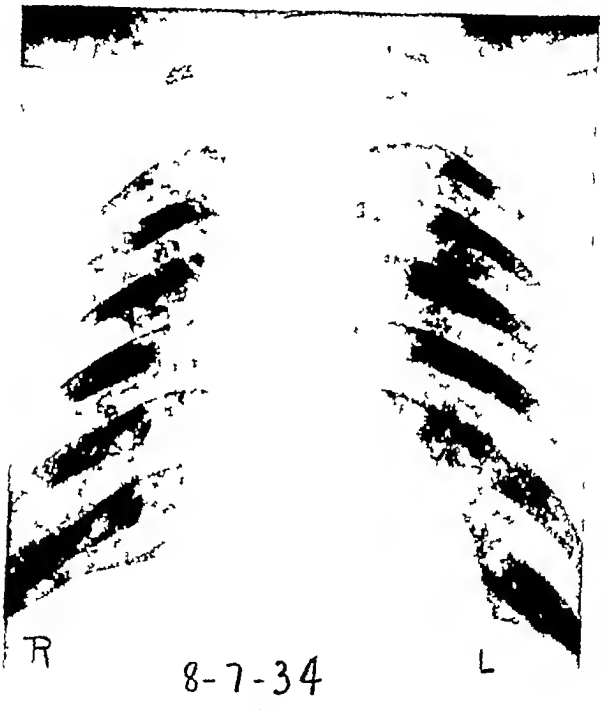


Fig 187 —x-Ray findings, August 7, 1934, a few weeks after the onset of pulmonary symptoms

both by physical examination and electrocardiographic study, found that his heart was perfectly normal He was inclined, at that time, to regard the complaint as a neuralgia, brought about by too much exposure to electric fans, both day and night The pain, however, continued and gradually he developed an annoying cough Having never had a

cough before in all his life, he assumed that it was probably due to an excessive consumption of tobacco and promptly stopped smoking At this time x rays were taken, and it was noted that he was running a fever, particularly in the evening, ranging as high as 102° or 103° F , blood tinged sputum had made its appearance, and it was finally decided, on the basis of physical signs and x ray evidence, that he had pulmonary tuberculosis of the left upper lobe (Fig 187) He went to a sanatorium in Southern Texas, where he remained for one month, running a constantly elevated temperature associated with some night sweats, moderate dyspnea, and *persistent deep pain* in his upper left chest It was at the end of a month s stay in the sanatorium that he decided to come to Baltimore since a definite diagnosis as to what was wrong had not been established Repeated examinations of his sputum had not revealed the presence of tubercle bacilli or other diagnostic findings

Admission Note—The patient did not look particularly ill, was not dyspneic, cyanotic or cachectic actually, he had lost not more than 3 or 4 pounds from his accustomed weight level There was no pallor to the mucous membranes, there were no skin eruptions, and no evidence of glandular enlargement could be detected anywhere Frequent coughing spells caused pain on the left side of his chest and in the left scapular region

Positive findings were essentially limited to the chest The right lung seemed normal throughout At the left apex anteriorly, and in back as far down as the midscapular area, there was slight percussion impairment, the breath sounds were somewhat bronchovesicular in type, and there were showers of fine and medium moist rales which did not disappear after expiratory cough The character of his breath sounds varied a bit from day to day, and at times they were so distant, particularly in front at the apex, as to suggest the possibility of atelectasis and some bronchial obstruction, though stridor was at no time noted The spleen and liver were not palpable His joints were normal There were no neurological abnormalities

His initial laboratory studies and special investigations can be summarized briefly, as follows

(*a*) *Blood Findings*—Red blood corpuscles, 4,680,000, hemoglobin, 88 per cent, white blood corpuscles, 28,000, of which 88 per cent were mature polynuclear cells, no pathologic leukocytes were found There were no eosinophils

(*b*) *Sedimentation Rate*—Thirty-five mm in thirty minutes

(*c*) *Agglutination reactions* for undulant fever, tularemia, typhoid, etc , were all negative

(*d*) *Blood cultures* were repeatedly negative

(*e*) *Blood Wassermann*, negative

(*f*) *Sputum* was mucopurulent in character, moderately abundant, not offensive, and definitely streaked with blood Many smears were examined for the tubercle bacillus, both before and after the use of concentration methods, with negative findings

(*g*) *x-Ray studies* included surveys of the teeth and sinuses, which were normal His initial chest film was interpreted by Dr C A Waters, as follows "There is consolidation of the left upper lobe, with a small cavity, and beginning changes in the upper portion of the lower left lobe The root shadows are increased on both sides The condition is probably tuberculous, but a lung abscess must be considered The picture does not suggest a new growth Hodgkin's disease cannot be excluded" (Fig 188)

Clinical Course—The patient ran a continuous fever of a somewhat remittent type throughout the entire period of his stay in the hospital Not infrequently he had drenching night-sweats His appetite and digestion were really excellent, and he had no symptoms whatsoever referable to his gastro-intestinal tract His leukocytes averaged around 30,000 and at times reached as high as 52,000, with an average of 90 per cent mature polynuclear cells, a consistent absence of abnormal leukocytes and a complete and persistent absence of eosinophils Repeated examinations of the sputum and cultures, both aerobically and anaerobically, yielded negative

findings for any specific fungus infection or Spirilla On September 26, October 9 and October 23, 1934, broncho scopic examinations were carried out by Dr E N Broyles, who could find no evidence of compression or tumor growth It is interesting that lipiodol did not enter the left upper lung satisfactorily, and also that following its instillation on

Fig 153—x Ray findings September 22 1934 Note the marked progression of pulmonary changes in approximately six week

October 23rd the patient experienced a marked sense of improvement and for nearly a week his temperature chart was practically normal

The problem in our minds had by this time narrowed itself down to the following probable conditions

(a) A pulmonary abscess involving the left upper lobe

(*b*) Some type of mycotic infection, not demonstrable, however, by any known method

(*c*) An unusual form of new growth

By reason of the consistently negative sputum findings, the character of the temperature chart, *x*-ray changes and persistent elevation of the leukocytes, we were convinced that we were not dealing with any form of tuberculosis, and for the same reasons the weight of opinion, including that of Dr Louis Hamman, who was called in consultation, favored a pulmonary abscess or its equivalent, namely, a diffuse bronchiectasis, which was somewhat suggested by the appearance of later *x*-ray plates There was no evidence of clinical improvement following the administration of neoarsphenamine, nor after the administration of fairly large amounts of potassium iodide, given both by mouth and intravenously, as a matter of fact, this particular drug upset the patient so much that its use was unfortunately discontinued

Artificial pneumothorax was started on October 28th, with two thoughts in mind First, that compression might possibly have some favorable therapeutic effect, and second, if it did not it would at least pave the way for contemplated chest surgery and a possible lobectomy Between October 28th and November 7th, a total of 4000 cc of air were injected by Dr George G Finney, and though a good collapse was obtained in the lower portion of the chest, it was apparent that the left upper lobe was densely adherent to the chest wall (Fig 189) Up to this time physical examination as well as *x*-ray findings of the right lung were essentially normal

On November 14, 1934, lobectomy was attempted by Dr William F Rienhoff, Jr The left upper lobe was found to be densely adherent to the chest wall, and decortication of the lung was all that could be accomplished at this time, for the patient went into either surgical or pleural shock and nearly died on the table It should be noted that a few days prior to his operation Dr Rienhoff had injected 200 cc of sterile bouillon into the left pleural cavity, to induce a granulation tissue reaction and minimize thereby the likelihood of any

postoperative empyema As a matter of fact, empyema at no time developed subsequent to his operation despite the fact that large amounts of purulent material were discharged from the left upper lobe through handling

By this time the patient showed manifest evidences of loss in weight, and had developed a secondary anemia Be

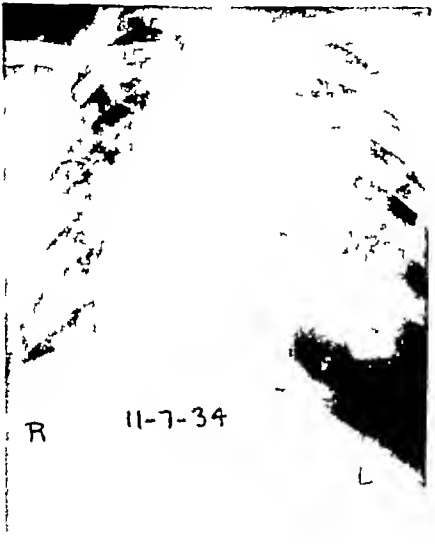


Fig 189—Note failure of collapse of left upper lobe after artificial pneumothorax. Lipiodol is seen in both lungs

tween November 8th and November 28th he received, in all eight transfusions of blood and entered the month of December with a red count of 4,480 000 a hemoglobin of 80 per cent and a white count of 47 000 His temperature range was unaffected by the surgical procedure and within a week or ten days following it there were evidences of distinct activity

in the right upper lobe and, to a less extent, in the lower lobes on both sides On December 3rd, following an attack of coughing, the patient became suddenly pale and died within two or three minutes

A postmortem was made by Dr W C Merkel within an hour after death Unfortunately, the examination was limited to the thoracic cavity An abstract of the autopsy protocol reads as follows

General inspection of the body revealed no recent or pronounced loss in weight, no skin abrasions, no subcutaneous glands and no pigmentation The mouth was very carefully examined, and neither the teeth nor mucous membranes showed any evidence of demonstrable infection One inch below the level of the left nipple there was an operative wound, beginning at the sternum and passing laterally to the posterior axillary line on the left In the axilla a rubber drain was encountered, which extended well into the pleural cavity

The left pleural cavity was filled with a gelatinous hemorrhagic fluid, containing yellowish flakes of a fibrinous exudate The left lung was collapsed Both parietal and visceral pleural surfaces were covered with a thick fibrinous exudate The apex of the left lung was adherent to the chest wall and was found to be considerably macerated, probably as a result of his recent operation The right lung was adherent to the parietal pleura along the posterior border and at the apex There was no fluid in the right pleural sac The upper and middle lobes were found completely consolidated, firm in consistency, and having the gross appearance of gray hepatization The pericardium was firmly adherent to the anterior chest wall, and the pericardial sac contained about 250 cc of a clear straw-colored fluid The heart itself was normal, weighed 250 Gm , and showed no gross evidence of any pathology

A clamp was placed on the trachea, about 2 inches above the bifurcation, and both lungs were removed *en masse* This was done in order to trace, if possible, the source of hemorrhage, which had apparently been the cause of death, since both bronchi were found to be filled with blood which had

clotted and could be traced into the bronchi of the second and third order on both sides The actual source of hemorrhage was not discovered The hilum and mediastinal lymph nodes were but moderately enlarged and not conspicuous, as one would expect to find with either pneumonia or tuberculosis None of the glands showed gross evidence of necrosis

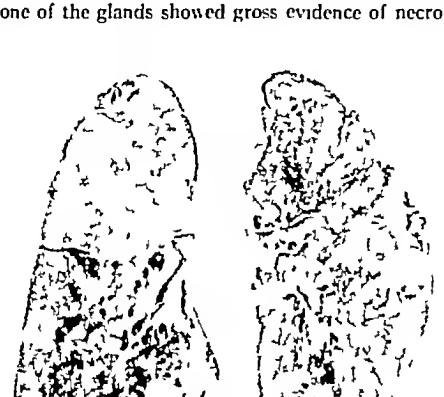


Fig 190—Cut surfaces of lungs Note extension of necrosis thickened pleura of left lung Lymph nodes show no involvement

The cut surfaces of the lungs are beautifully illustrated in the photograph (Fig 190) There were numerous discrete circumscribed yellowish necrotic areas averaging from ½ to 3 cm in diameter found in the lower lobe of each lung many of them also confluent The upper left lobe showed no striking necrosis in the parenchyma but numerous sinus tracts extended into the substance of the lung from the pleural surface This suggested that the process had actually cleared up

to some extent by drainage into the pleural cavity The right lung showed marked consolidation and necrosis of both upper and middle lobes, and in the lower lobe there were recent necrotic areas, all of which communicated with the bron-

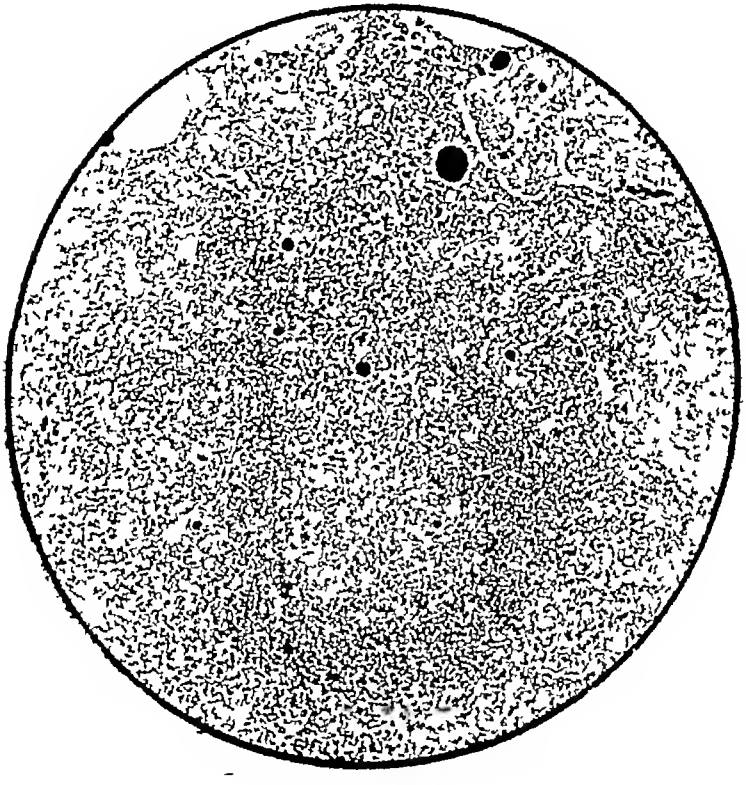


Fig 191 —Low magnification photomicrograph of typical lung lesion, showing the inflammatory reaction characterized by coagulation necrosis The necrotic area is surrounded by a zone of infiltrating cells chiefly of the polymorphonuclear type There are also large mononuclears, many containing fat droplets The early lesions are all confined to the bronchioles

chioles An opening was made through the diaphragm and a biopsy was obtained from the spleen and liver, both of which were found to be normal

Numerous fresh smears were made from the exudate and necrotic tissue obtained from the discrete areas and exudate

on the pleural surfaces Unstained as well as stained preparations showed slender nonseptate true branching mycelia, which did not retain Gram stain uniformly, nor were they acid fast In one preparation typical ray fungi, showing radial arrangement of club shaped bodies, were found The exudate in which these bodies were encountered was obtained from an area of encapsulated necrosis in the apex of the left lung Aerobic cultures were negative Anaerobic cultures, carried

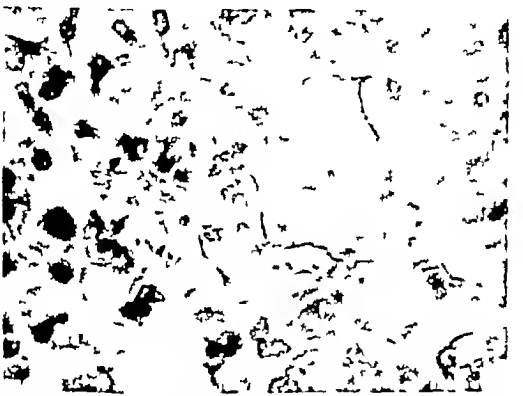


Fig 192—Oil immersion photomicrograph showing the branching mycelia and irregularity of staining in them

on by Dr Hachtel at the University of Maryland ultimately yielded a pure culture of Actinomyces bovis

The summarized final autopsy report reads as follows

1 Primary pulmonary actinomycosis, involving the upper left lobe, with extension into all of the other lobes of both lungs.

2 Postoperative thoracotomy wound

3 Atelectasis of the lower left lobe

4 Pulmonary hemorrhage with asphyxiation

DISCUSSION

(A) **Historical Résumé**—In 1877, Bollinger noted a peculiar disease occurring in cattle, which was characterized by hard swellings, particularly of the tongue and jaw His friend, Harz, a botanist, recognized in the discharge from these lesions a true and apparently new fungus, and to it gave the name Actinomyces bovis The fungus in question was first successfully cultivated anaerobically in 1891, by Wolff and Israel Almost at the same time Bostroem isolated another aerobic strain, to which the name Actinomyces graminis was given Though for years this organism was presumed not to be etiologically related to infection in man, this has recently been questioned by the report of a case of pulmonary infection by Biggart All the weight of accumulated evidence, however, points to the fact that actinomycotic infection, as it occurs in either cattle or man, is caused mainly by the Actinomyces bovis, a nonacid-fast, nonmotile, gram-positive organism, which shows characteristic true branching

In their recent book on bacteriology, Topley and Wilson give the most satisfactory classification of the various types of Actinomyces as they are at present recognized Most of the members of this fungus group are aerobic and lead a strictly saprophytic existence on grains, grasses and in the soil, and a number of them are known to be pathogenic in their effect upon plants Though formerly it was believed that infection in man occurred through the chewing of grains or straw, or as a result of contact with infected animals, this view now seems to be refuted, since the anaerobic strain has not been found outside of the human body The essential point of evidence in favor of an exogenous method of human infection has thus far not been conclusively produced, namely, that Actinomyces bovis exists as a saprophytic parasite That this evidence will ever be forthcoming seems unlikely, for it is now recognized that the organism is really a very delicate anaerobe which can be cultivated only with difficulty and at body temperature, and, so far as is known, does not produce resistant spores Contagion for actinomycosis has not been demonstrated

(B) Incidence.—From all data available, it is apparent that actinomycotic infection of man is a rare disease. Lord, writing in 1925, makes the statement that only 65 cases occurred among 122,408 medical and surgical admissions to the Massachusetts General Hospital (0.053 per cent). In the same year Sanford and Voelker, from the Mayo Clinic, compiled statistics on a total of 670 cases which they were able to gather from all portions of the United States. No extensive compilation has been made since.

In all of the series reported approximately 80 per cent of the cases occur in males, chiefly young adults; but instances are on record of infection in children between the ages of one and ten. Though on first glance country folk supply the majority of cases, the disease is by no means limited to rural dwellers. All statistics are in accord with the statement that nearly 60 per cent of the cases occur primarily in the cervicofacial region, approximately 18 per cent appear to develop primarily in the abdomen, and finally the *thoracic* type is found in about 14 per cent, but it should be noted that this group includes not merely infections of the lungs but of the chest wall as well. Rarer forms of the disease may occur anywhere, though it appears that actinomycotic infection of bone is very rare in human beings.

Granted that the incidence of the disease is low, it is safe to say that authentic instances of *primary* pulmonary actinomycosis are exceedingly rare. In most instances in which pulmonary actinomycosis has occurred the pulmonary lesions have developed secondary to infection elsewhere. The infection apparently is spread through the blood channels rather than the lymphatic system, and clinically it is noteworthy that glandular enlargement is strikingly absent in almost all forms of the disease.

In a series of 12,000 consecutive autopsies at the Johns Hopkins Hospital, there were only eight instances in which the cause of death was actinomycosis, and of these only one (the case recently reported by Biggart) was regarded as primarily a case of pulmonary infection. When pulmonary in-

volvement does occur, the lower portions of the lungs are most commonly involved

(C) **Diagnosis**—The diagnosis of actinomycotic infection is positive and absolute only by the finding of the so-called "characteristic sulphur granules," or by cultivation of the organism itself In the case herewith presented, the question naturally arises as to why the etiologic agent was not demonstrable until after death The answer probably lies in the fact that much work remains to be done in the cultural methods as they may apply to this group of organisms Many technical difficulties are encountered in their isolation The lesions are almost invariably infected by other invading organisms, and the so-called "granules" from old lesions not infrequently prove to be sterile According to many opinions, particularly that advanced in the monographic work of Homer Wright, granule formation is much more outspoken in bovine than in human lesions, and in the latter he states that they may be entirely absent Their formation in any case is most pronounced in lesions in which there is considerable development of connective tissue, "and in which the progress of the disease is slow, with manifest resistance on the part of the tissue to the spread of the process, while in relatively rapidly progressive cases or those in which there is little evidence of resistance on the part of the tissue to the infection, clubs may be wanting on the granules" Wright further concludes that club formation is a protective device adopted by the organism to protect, for a time, the main mass of the fungus constituting the granule from the destructive action of the tissue cells and juices Numerous authorities, and particularly Turner, call attention to the fact that the demonstration of the organism in the sputum is by no means an easy matter, and it is more than likely to be overlooked in any ordinary method of so-called "routine sputum examination" In suspected instances it is wise to mix the sputum with normal salt solution, thoroughly shake the mixture, and granules, if present, will fall to the bottom of the receptacle and can be fished out, crushed between glass slides and properly identified

Moreover, one of the characteristics of the mycelia themselves is their extreme pleomorphism, with the result that they may appear as irregularly staining filaments, cocci, or actually present the appearance of pure streptococci

There are no characteristic blood findings which are of real diagnostic value in this type of infection All forms of the disease are apparently characterized by an elevation of the leukocytes, but no case has been encountered in the literature in which the elevation was so consistently high as in the one herewith reported Other types of blood diagnostic methods as yet are not available, and Topley and Wilson emphasize the fact that in our search for further knowledge about actinomycotic infections, not only do we need better means for isolation and identification, but also the development of specific agglutination reactions At the present time there are none

Up to the present time no characteristic diagnostic picture has been recognized from a roentgenological point of view Kirklin and Hefke recently reported a series of 14 cases, analyzed as to their x ray findings Various types of pleural and pulmonary changes were observed and described by them, consisting mainly of enlargement of the hilum, infiltrative strands radiating into the lung from the hilum, localized consolidation in one or more lobes, pleural thickening, dense pleuritic adhesions and fluid in the pleura The lack of uniformity in the x ray findings is emphasized by all writers A purely roentgenological differential diagnosis from chronic abscess of the lung, with or without empyema, from chronic tuberculosis or from chronic empyema with thickened pleura seems at present impossible In general, it may be said that from a roentgenological viewpoint actinomycosis more frequently involves the lungs from the hilus downward, while tuberculosis usually extends from the hilus upward In an instance such as this in which the primary involvement was at the apex of the lung, the diagnostic difficulties become that much greater

In the absence of any specific diagnostic findings from a

laboratory or *x*-ray point of view in an instance such as this, are there any clinical phenomena which might lead to an earlier diagnosis in a similar case? There are a few which are at least worth consideration First and foremost, perhaps, was the early onset and continuous persistence of pain, probably referable to early involvement of the pleura, and pain of a nature not ordinarily encountered in an apical tuberculosis The association of this constant pain with a blood-tinged sputum constantly negative for tubercle bacilli, occurring in association with a constant elevation of temperature and a high leukocyte curve, would in a similar instance lead me to assume an actinomycotic infection, even in the absence of the finding of sulphur granules or diagnostic sputum cultures There are no physical signs by which a differential diagnosis can be made

(D) **Prognosis and Treatment**—All authors agree in the statement that the prognosis in the thoracic or pulmonary form of actinomycosis is bad There are very few cases on record in which pulmonary involvement has been followed by recovery Obviously, if any form of treatment is to be of avail it must be instituted at just as early a date as possible All the weight of experience seems to favor surgical excision of diseased tissue, combined with the administration of large amounts of potassium iodide, administered over a long period of time In the present instance iodides were so badly tolerated that it seemed almost incumbent to discontinue their administration, but in the light of subsequent developments, it might perhaps have been wiser to have administered iodides in large amounts, intravenously, regardless of the symptoms which they provoked There is no evidence to suggest that the arsenicals are of any therapeutic value in this disease With improvement in thoracic surgery, it is possible that cure might be effected by a very early lobectomy, yet from the experience gained in this case, one would have to assume that the likelihood of cure by this radical procedure is at present very remote

Recent reports summarized in the current Year Book of

Radiology report favorable results by treatment with either x ray or radium Those lesions which have thus far responded favorably to these forms of treatment have been preeminently of the cervicofacial type Abdominal actinomycosis has been treated less successfully, and "roentgen treatment for thoracic lesions shows still poorer results, the mortality for the cases collected being over 80 per cent" It is claimed that the poor results may possibly be accounted for by the inadequate dosage, and that with improvement in the technic of deep therapy the prognosis will be very much better

BIBLIOGRAPHY

Wolff and Israel Virch Arch 1891 126 11
Bostroem Ziegler s Beitrage 1890 9 1
Biggart Bulletin of the Johns Hopkins Hospital 1934 54 165
Topley and Wilson The Principles of Bacteriology and Immunity 1934 1 242 2 787
Lord Medical Clinics of North America 19 5 1485
Sanford and Voelker Archives of Surgery 1925 11 809
Wright Journal of Medical Research 1905 13 349
Turner Radiology 1926 39
Kirklin and Ifeffe American Journal of Surgery 1931 13 1
Waters and Kaplan Year Book of Radiology 1934

INDEX TO VOLUME 18

Abdomen surgical emergencies of *July* 63
surgical extra-abdominal lesions simulating x ray diagnosis, *March* 1439
Abdominal affections acute as cause of gastric pain, *July* 95
roentgen diagnosis *March* 1421
contusions, with rupture of solid viscus *July* 66
with visceral injury *July* 64
distention in pneumonia in children treatment, *Nov* 824
infections acute as surgical emergencies, *July* 73
injuries roentgen diagnosis *March* 1437
obstruction as surgical emergency *July* 76
pain and tenderness in mucous colitis *Nov* 894
roentgen diagnosis of extra-abdominal lesions causing *March* 1439
strangulation as surgical emergency, *July* 76
traumatism as surgical emergency *July* 63
walls, wounds of as surgical emergency *July* 71
Abducens paralysis in anterior polio myelitis, *July* 21
Abscess appendiceal rupture of as surgical emergency *July* 73
of lung *Sept* 439 *Nov* 825 See also *Lung abscess of*
of spinal epidural area *July* 287
Acetarsone See *Stovarsol*
Acid base disturbances in infants and children *Jan*, 1205
Acidophilic pituitary adenomas *July* 255
Acidosis in infants and children with gastro-intestinal disturbances chronic nephritis and diabetes mellitus *Jan* 1205
Kussmaul breathing in *Jan* 1209
Acne vulgaris *March* 1465
Acneform eruption of allergic origin *March* 1461
Actinomycosis pulmonary *May* 1 See also *Lung actinomycosis of*
Addison's disease gastro-intestinal symptoms *Sept* 513
Adenoma pituitary acidophilic, *July* 255
basophilic, *July* 256
chromophobe *July* 254
Adenopathies classification, *Nov* 640
other tumefactions and differentiation *Nov* 41
symposium on *Nov* 633
treatment, with special reference to irradiation *Nov* 703
Adenopathy affecting primarily the corticomedullary portion of the lymph gland *Nov* 657
carcinomatous *Nov*, 690
treatment *Nov* 718
infiltrative type *Nov*, 685
originating primarily in reticuloendothelium of lymph gland *Nov* 669
secondary to anterior poliomyelitis *Nov* 646
to anthrax *Nov*, 645
to eczema *Nov* 644
to favus *Nov*, 644
to local infection *Nov* 642
to primary hematopoietic disease, *Nov* 691
to rheumatic fever *Nov* 645
to rubella *Nov*, 645
to scarlet fever *Nov* 644
to systemic infection *Nov* 641
to tuberculosis, *Nov* 647
to tularemia *Nov* 645
to typhoid fever *Nov* 646
Adiposity of heart *Sept* 471
Adiposogenital dystrophy *July* 243
dietotherapy *July* 251
estrin therapy *July* 249
pituitary therapy *July* 247
roentgen therapy *July* 247
symptoms *July* 243
thyroid therapy *July* 248
treatment *July* 246
Adnexal disease as cause of leukorrhea *May* 1695
Adrenal cortex, tumors of in children *March* 1463
gland carcinoma of pluriglandular syndrome associated with *May* 1374

Adult serum, pooled, in prophylaxis of anterior poliomyelitis, *July*, 35
in treatment of anterior poliomyelitis, *July*, 43
whole blood in prophylaxis of anterior poliomyelitis, *July*, 35
reactions, *July*, 37
Air swallowing by person with psychopathic ancestry, *Sept*, 546
Albuminuria, febrile, *March*, 1334
Alcohol addiction predisposing to gout, *Jan*, 1004
injections in tuberculous laryngitis, *March*, 1380
Aleukemic reticulosis, *Nov*, 673
Alkalosis in infants and children with gastrointestinal disturbances, chronic nephritis and diabetes mellitus, *Jan*, 1205
Allergic dermatitis, *March*, 1253, 1254
diseases, *March*, 1227
diagnosis, *March*, 1231
examination of patient, *March*, 1229
history taking, *March*, 1228
intracutaneous test, *March*, 1230
patch test, *March*, 1231, 1257
scratch tests, *March*, 1230
treatment, *March*, 1232
nasal disease *March*, 1233 1235, 1245
radium treatment, *March*, 1250
rhinitis, *March*, 1234, 1235, 1245
therapy in bronchial asthma, 136
Allergy in diseases of skin, *March*, 1253
Amebiasis, diagnosis, *Sept*, 420
intestinal, *Nov*, 851
arsenicals in, *Nov*, 855
bismuth in, *Nov*, 857
emetine in, *Nov*, 854
oxyquinoline in, *Nov*, 856
pathology, *Nov*, 852
symptomatology, *Nov*, 852
treatment, *Nov*, 851, 853
of chronic cyst passer, *Nov*, 858
probable, case representing, *Sept*, 418
treatment, *Sept*, 420
unusual case, *Sept*, 537
Amebic dysentery, *Nov*, 851
Amenorrhea, *Nov*, 772
causes, *Nov*, 772, 774
diagnosis, *Nov*, 774
diet and hygienic measures in, *Nov* 780
endocrine therapy, *Jan*, 1157
evaluation of, *Nov*, 782, 788
in adiposogenital dystrophy, *July*, 243
Amenorrhea in adiposogenital dystrophy, treatment, *July*, 246
in pituitary adenomas, *July*, 254
stimulating x-ray treatment, *Nov*, 782
treatment, *Nov*, 779
Amidopyrine in rheumatic heart disease in children, *May*, 1563
Amniotin, *Jan*, 1146
in adiposogenital dystrophy, *July*, 250
Amyloidosis, diffuse, of unknown etiology, *Sept*, 413
Anaphylaxis See *Allergic diseases*
Anatomical tubercle, *July*, 321
Anayodin in intestinal amebiasis, *Nov*, 856
Anemia in inoperable carcinoma of stomach, treatment, *Jan*, 1183
lymphatica, *Nov*, 673
nephritic, treatment, *Nov*, 876
pernicious, chronic pancreatitis complicating *Sept* 519
concomitant conditions, *Jan*, 941
diagnosis *Jan*, 935
excess pigment metabolism in, infrequency of *Jan*, 941
gallbladder disease in, *Jan*, 939
long standing indigestion in, *Jan*, 939
onset symptoms and time for diagnosis, *Jan*, 936
precipitation of deficient state, *Jan*, 943
treatment with equine liver extract subcutaneously, *Sept*, 391
with preparation of liver and stomach (extralin), *Sept*, 385
with intermittently painful joints and splenomegaly, *Jan*, 1053
Aneurysm, false, spontaneous, of popliteal artery *Sept*, 613
of aorta, dissecting, electrocardiographic signs simulating coronary occlusion, *July*, 226
spontaneous *Jan*, 1117
case reports, *Jan*, 1118
clinical manifestations, *Jan*, 1132
physiologic implications *Jan*, 1136
coronary thrombosis and, differentiation, *Jan*, 1138
etiology and mechanism, *Jan* 1125
frequency, age and sex incidence, *Jan*, 1131
laboratory findings, *Jan*, 1136

Aneurysm of aorta dissecting spontaneous, signs *Jan* 1134
symptoms *Jan* 1133
Hodgkin's disease and differentiation *Nov* 678
Angina of decubitus *March* 1272
pectoris *Nov* 753 *May* 1507
atypical cases, diagnosis, *March* 1263
clinical manifestations *March* 1265
in syphilis of heart *May* 1538 1541 1543
increase in *March* 1263
radicular syndrome simulating *March* 1266, 1270
theories of origin *May* 1510
treatment *Nov* 755 *May* 1509
surgical measures *May* 1509
Vincent's *May* 1711 1712
Anginal pain heart failure manifested by *Nov* 753
treatment *Nov* 755
Angioneural arthrosis *Jan* 997
Ankle joint arthritis of *Jan* 965
physiotherapy in *Jan* 1018
Anterior lobe hypopituitarism *July* 252
pituitary extract in obesity *Jan* 1199
poliomyelitis See *Poliomyelitis anterior*
Anthracosis, *Nov* 686
Anthrax, adenopathy secondary to *Nov.*, 645
Antiseptics use of in acute sinusitis *July* 373
Antitoxin treatment of erysipelas *Nov* 861
observations on 4698 patients *Nov* 861 864
Antophysin *Jan* 1146
Antuitrin in treatment of Fröhlich's syndrome *March* 1452
Antuitrin S *Jan* 1146
in treatment of adiposogenital dystrophy *July* 248
Anuria in acute nephritis, treatment *Nov.*, 840
Aorta aneurysm of dissecting electrocardiographic signs simulating coronary occlusion *July* 226
spontaneous *Jan* 1117
Hodgkin's disease and differentiation, *Nov.*, 678
Aortic insufficiency syphilitic *May* 1541 1541
Aortitis syphilitic *May* 1534 1539
Appendiceal abscess, rupture of as surgical emergency *July* 13
Appendicitis acute, as cause of gastric pain *July* 95
early recognition *March* 1489
in children *March* 1492
pneumonia and differentiation *July* 200
roentgen diagnosis *March* 1436
symptoms and diagnosis early *March* 1489
with infection as surgical emergency *July* 13 74
as cause of indigestion *July* 90
Aquamedin in diabetes mellitus *May* 1606
Arrhythmia *May* 1545
sinus treatment *May* 1547
treatment *May* 1545
Arsenic in chorea *Jan* 1088
in myelogenous leukemia *Nov.*, 773
Arsenicals in intestinal amebiasis *Nov* 855
Arsphenamine in Vincent's disease *May* 1 19 1720
reactions in treatment of syphilis of heart *May* 1533
Arteriosclerotic occlusion of left subclavian artery *Sept* 629
Arthritis acute complicated by asthma and hay fever *Jan* 996
by rheumatic fever *Jan* 989
diagnosis *Jan* 989
gonococcal *Jan* 991
syphilitic *Jan* 994
atrophic See *Arthritis chronic infectious (atrophic)*
chronic *July* 104
blood transfusion in *July* 139
chemical studies in *July* 115
circulatory disturbances in *July* 115
climatotherapy in *July* 130
colonic irrigations in *July* 134
diet in *July* 121
drugs in *July* 137
etiology *July* 110
examination in *July* 119
exercise in *July* 136
foci of infection in *July* 111
removal *July* 130
historical *July* 10
importance of problem *July* 109
incidence *July* 10
infectious (atrophic) *July* 112
114
arthrodesis in [illegible] 850
arthroplasty in [illegible] 850
characteristic deformities and their prevention See 849

Arthritis, chronic, infectious (atrophic), correction of deformities, *Sept*, 568
gout and, *Jan*, 1009
results of failure or neglect in care of, *Sept*, 549
rules of exercise in, *Sept*, 564
therapeutic measures, *Sept*, 565
traction and manipulation in, *Sept*, 569
joint changes in, *July*, 112, 114
massage in, *July*, 124
pathology, *July*, 112
physiotherapy in, *July*, 125
posture in, *July*, 127
rest in, *July*, 121
symptoms, *July*, 117
treatment, *July*, 118
vaccines in, *July*, 129
degenerative, *July*, 112, 114, 117, 118, *Jan*, 947, 1014
Charcot joints and, *Jan*, 951
diagnosis *Jan*, 947
erythrocytic sedimentation test in, value, *Nov*, 913
hemophilia as cause, *Jan*, 952
mechanical trauma as cause, *Jan*, 971
occupation and, *Jan*, 949
pathology, *Jan*, 947
physiotherapy in, *Jan*, 1015
rheumatic fever and, *Nov*, 759
static or postural defects as cause, *Jan*, 950, 976–980
trauma as cause, *Jan*, 973
hypertrophic. See *Arthritis, degenerative*
in children, *May*, 1673
case reports, *May*, 1676
factors distinguishing it from adult disease, *May*, 1674
of ankle joint, *Jan*, 965
physiotherapy in, *Jan*, 1018
of elbow joint, *Jan*, 954
physiotherapy in, *Jan*, 1020
of finger joints, *Jan*, 955
physiotherapy in, *Jan*, 1019
of foot joints, *Jan*, 966
of hip joint, *Jan*, 962
physiotherapy in, *Jan*, 1019
of knee joint, *Jan*, 964
physiotherapy in, *Jan*, 1016
of metacarpophalangeal articulations, physiotherapy in, *Jan*, 1018
of sacroiliac joint, *Jan*, 961
lumbosacral arthritis and, differentiation, *Jan*, 962
of shoulder joint, *Jan*, 953
Arthritis of shoulder joint, physiotherapy in, *Jan*, 1021
of spine, *Jan*, 955, *March*, 1347
See also *Spine, arthritis of*
of temporomandibular joints, *Jan*, 952
of wrist joint, *Jan*, 954
physiotherapy in, *Jan*, 1020
physiotherapy in, *Jan*, 1013
proliferative, *July*, 112, 117
physiotherapy in, *Jan*, 1015
rheumatoid See *Arthritis, degenerative*
symposium on, *Jan*, 945
Arthrodesis in chronic infectious arthritis, *Sept*, 569
Arthroplasty in chronic infectious arthritis, *Sept*, 570
Arthrosis, angioneural, *Jan*, 997
Artificial feeding of newborn, *March*, 1416
Asphyxia neonatorum, *March*, 1407
Aspiratory type of pulmonary abscess, *Sept*, 430
Asthma, arthritis in, *Jan*, 996
bronchial, allergic therapy, *July*, 136
bacterial, treatment, *July*, 138
cutaneous tests in, *July*, 134
diagnosis, *July*, 134
drugs in, *July*, 139
glucose intravenously in, *July*, 140
mechanism of attack, *July*, 135
pollen, treatment, *July*, 137
vaccine therapy, *July*, 139
treatment, *July*, 133, 136
nocturnal, in heart failure, treatment, *Nov*, 747
Ataxic type of anterior poliomyelitis, *July*, 22
Atony, intestinal, colonic irrigations in, *May*, 1614, 1619
Atopic eczema, *March*, 1253, 1254
Atopy See *Allergic diseases*
Atresia of gastro-intestinal tract in newborn, *March*, 1408
Atrophic arthritis *July*, 112, 117
gout and, differentiation, *Jan*, 1009
Atropine in acute sinusitis, *July*, 372
Auricular fibrillation, *July*, 343
blood pressure in, *July*, 347
diagnosis, *July*, 346
differential diagnosis, *July*, 346
digitalis therapy in, *July*, 348, *Nov*, 749 *May*, 1553, 1583
diuresis in, *July*, 350
etiology, *July*, 343
physiology, *July*, 344

Auricular fibrillation prognosis *July* 350
quinidine therapy *July* 349 *Nov.*, 751 *May* 1554
symptoms, *July* 345
treatment *July* 348 *May* 1553
flutter digitalis therapy *May* 1554 1584 1586
treatment *May* 1553
precocious systoles treatment *May* 1551
Autaresis in anterior poliomyelitis *July* 8 35
Autosomes in transmission of diabetes *July* 213
Avitaminosis in mucous colitis treatment *Nov.*, 905
Azotorrhea in chronic pancreatitis diagnostic value *Sept* 519

Bacillary dysentery chronic, *March* 1327
treatment *March* 1329
Bacillus tuberculosis identifying in cutaneous tuberculosis *July* 311
Back gibbus, *Nov* 651
spasticity and rigidity of in anterior poliomyelitis *July* 18 27 28
Backache *Jan* 980 *March* 1343
due to arthritis of spine *March* 1347
to postural deformities, *March* 1345
to spinal deformities of poliomyelitis *March* 1349
of rickets *March* 1350
of tuberculosis *March* 1351
etiology *March* 1343
pelvic, *Jan* 982
Bacterial endocarditis acute, treatment *May* 1516 1517
subacute treatment *May* 1521
type of bronchial asthma, *July* 138
Basophilic pituitary adenomas *July* 256
Basophilism pituitary with suprarenocortical syndrome *Sept* 411
Bath saline in anterior poliomyelitis *July* 57
Bazin's disease *July* 370
Behavior problems of children *May* 1643
Bence Jones proteinuria complicating hyperparathyroidism *Jan* 1109
Bicarbonate buffer effect of on acid base balance *Jan.*, 1708
Bile culture *July* 175
Biliary drainage *July* 161
diagnostic value *July* 170
Biliary drainage specimens cellular elements *July* 167
crystallography *July* 171
food residues in *July* 174
macroscopic appearances *July* 170
microscopy *July* 170
parasites in *July* 173
shaggy mucus in *July* 173
technic, *July* 168
therapeutic value *July* 174
Bilious headache See *Migraine*
Birth injuries *March* 1404
Bismuth in intestinal amebiasis *Nov* 85
in Vincent's disease *May* 1720
Blackheads *March* 1466 1467
Bladder rupture of as surgical emergency *July* 10
Bleeding postmenopausal *Nov* 783
preclimacteric *Nov* 783 783
puberty *Nov* 783 783
Blood complement fixation test in visceral infection *July* 148
cultures in acute fevers technic *Sept* 573
in anterior poliomyelitis *July* 23
in sputum as symptom of acute heart failure in presence of mitral stenosis *Nov* 91
plasma normal composition of *Jan* 1206
pressure in auricular fibrillation *July* 347
transfusions in anterior poliomyelitis *July* 41
in chronic arthritis *July* 178
in pneumonia in children *Nov* 819
whole adult in prophylaxis of anterior poliomyelitis, *July* 35 36
reactions *July* 3
Breast feeding of newborn *March* 1413
Breasts of newborn secretion from *March* 1413
Breath, shortness of in rheumatic heart disease in children *May* 1580
Breathing Kussmaul in acidosis *Jan* 1209
Bright's disease *Nov* 807
Brill Symmers disease *Nov* 10
Bronchial asthma *July* 133 see also *Asthma, bronchial*
pneumonia See *Bronchopneumonia*
Bronchiectasis *Jan* 1011
collapse therapy *Jan.*, 1015
complicating pneumonia in children treatment *Nov* 815

Bronchiectasis, diagnostic measures, *Jan*, 1041, 1050
lobectomy in, *Jan*, 1047
pain of three years' duration preceding operation, *Jan*, 1049
treatment, *Jan*, 1045, 1050
Bronchopneumonia in infants and children, *Sept*, 451
oxygen therapy, *March*, 1488
Bronchoscopy in bronchiectasis, *Jan*, 1044
Bronchus, plugging of, in pneumonia in children, treatment, *Nov*, 825
Brudzinski's neck reflex in anterior poliomyelitis, *July*, 26
Buffer effect of bicarbonate on acid base balance, *Jan*, 1208
Bulbar paralysis in anterior poliomyelitis, *July*, 21
treatment, *July*, 47

CACHEXIA, pituitary *July*, 253
Calcium bilirubinate pigment in biliary drainage specimen, *July*, 171
Camps for cardiac children, *March*, 1479, 1480
Caput succedaneum, *March*, 1408
Carbarsone in intestinal amebiasis, *Nov*, 856
Carbohydrate diet, liberal, in diabetes mellitus, *Nov*, 831
Carcinoma complicating hereditary diabetes, *July*, 276
of endometrium as cause of leukorrhea, *May*, 1699
of larynx, tuberculosis of larynx and, differentiation, *March*, 1378
of lung, abscess secondary to, *Sept*, 449
of pancreas body, *March*, 129
and tail, *March*, 1306
head, *March*, 1311
symptoms, *March*, 1312, 1315
tail, with carcinomatosis of peritoneum and omentum, *March*, 1309
of stomach as cause of indigestion, *July*, 89
found at operation after prolonged medical treatment of ulcer, *Sept*, 505
gastric pain in, *July*, 99
inoperable, anemia in, treatment, *Jan*, 1183
of suprarenal gland, pluriglandular syndrome associated with, *March*, 1367
Carcinomatous adenopathy, *Nov*, 690
treatment, *Nov*, 718
Carcinomatous polyp of sigmoid causing intussusception, *Sept*, 539
Cardiac See *Heart*
Carditis, *April*, 1515
rheumatic, treatment, *Nov*, 742
Cauterization of cervix for leukorrhea, *May*, 1704
Cerebral hemorrhage in newborn, *March*, 1404
type of anterior poliomyelitis, *July*, 22
Cerebrospinal fluid in anterior poliomyelitis, *July*, 23
Cervical lymph glands, syphilis of, *Nov*, 654
tuberculosis of, *Nov*, 648
spine, arthritis of, *Jan*, 959
physiotherapy in, *Jan*, 1021
Cervix, cauterization of, for leukorrhea, *May*, 1704
dilatation of, for dysmenorrhea, *March* 1279
lesions of, leukorrhea due to, *May*, 1700
Chalicosis, *Nov*, 686
Chancre, tuberculous, *July*, 321
Chancroid, glandular enlargement in, *Nov*, 655
Charcot joints, *Jan* 951
Children, appendicitis in, *March*, 1492
arthritis in, *May*, 1673
behavior problems, *May*, 1663
cardiac, convalescent care, *March*, 1471
endocrine disorders in, with particular reference to treatment, *March*, 1443
intellectually inferior, *May*, 1665
neuropathic constitutions in, *May*, 1666
pneumonia in, *Sept*, 451
treatment, *Nov*, 811
rheumatic heart disease in, management, *Jan*, 1067, *March*, 1471, *May*, 1559
temperament or disposition in, *May*, 1668
Chloroma, *Nov*, 685
Cholecystitis, acute, pneumonia and, differentiation, *July*, 200
Cholesterin crystals in biliary drainage specimen, *July*, 171
Chondrosarcoma complicating hyperparathyroidism, *Jan*, 1109
Chorea, *Jan* 1081
Fowler's solution in, *Jan*, 1088
nirvanol in, *Jan*, 1089
sedatives in, *Jan*, 1089
stramonium datura in, *Jan*, 1090
Sydenham's, *Jan*, 1081

Chorea treatment, *Jan.*, 1031
typhoid paratyphoid vaccine in *Jan* 1090
Christie's modification of Van Slyke Binger vital capacity test *May* 1689
Chromophobe pituitary adenoma *July* 254
Chromosomes, sex in transmission of diabetes *July* 273
Circulatory disturbances in chronic arthritis *July* 115
function vital capacity as test present status *May* 1685
Claudication intermittent effect of tissue extracts on *Sept* 609
Climatotherapy in chronic arthritis *July* 130
Clothing of newborn *March* 1418
Colitis, mucous *Nov* 889
abdominal pain and tenderness in *Nov* 891
avitaminosis in treatment *Nov* 905
colic in treatment *Nov* 903
colonic irrigations in *May* 1614 1619
constipation in *Nov* 896
treatment *Nov* 905
diagnosis *Nov* 901
diet in *Nov* 901
dislodgment of mucus *Nov* 901
etiology *Nov* 889
flatulence or gas distress in *Nov* 895
gastric hyperirritability in *Nov* 895
genito-urinary symptoms *Nov* 897
intestinal toxemia in *Nov.*, 896
nervous and psychic symptoms *Nov* 897
treatment *Nov* 907
pathology *Nov* 890
signs and symptoms, *Nov* 891
treatment *Nov* 903
between attacks of colic or when there is no colic, *Nov* 904
of attacks of colic, *Nov* 903
of nervous or psychic manifestations *Nov* 904
ulcerative chronic *Sept* 535
unusual metabolic disturbance with edema complicating *Sept* 529
colonic irrigations in *May* 1611
nonspecific (idiopathic) *March* 1319 *May* 1631
diagnosis, *March* 1321 *May* 1637
Colitis ulcerative, nonspecific (idiopathic) diet in *March* 1322
etiology *March* 1319 *May* 1632
incidence *May* 1634
pathology *May* 1634
surgery in *March* 1327
symptomatology, *May* 1634
treatment *March* 1321 *May* 1639
unusual case report *May* 1642
vaccine treatment *March* 1325
Collapse therapy in bronchiectasis *Jan* 1015
Colon diseases of as cause of epigastric distress *March* 1289
functional disorders *Nov.*, 883 885
as cause of indigestion *July* 87 88
hyperirritable *Nov* 887
diagnosis *Nov* 888
symptoms *Nov* 887
treatment *Nov.*, 888
physiology of *Nov* 883
polyps of multiple treatment *May* 1642
ulcerative conditions treatment *March* 1319
Colonic irrigations *May* 1611
contraindications *May* 1674
history of *May* 1611
in chronic arthritis *July* 121
indications *May* 1616
limitations *May* 1620
technic *May* 1621
value *May* 1613
Coma diabetic, with acidosis in children *Jan* 1121
Comedones *March* 1465
Common duct stone in simulating gastro intestinal disease *Sept* 500
Complement fixation test of blood in visceral infection *July* 148
Congenital abnormalities in newborn *March* 1408
cyst of lung abscess of lung caused by *Sept* 411
heart failure electrocardiographic signs simulating coronary occlusion *July* 22 228
Constipation colonic irrigations in *May* 1615 1617
in acute appendicitis *March* 1431
in mucous colitis *Nov* 896
treatment *Nov* 905
Constitution (Graves) *Nov* 905
neuropathic in children *May* 1665

Constitutionally inadequate food sensitive gifted man with poor nervous heredity, *Sept*, 544
Contusions, abdominal, with rupture of solid viscus, *July*, 66
with visceral injury, *July*, 64
Convalescent care of cardiac children, *March*, 1471
serum in prophylaxis of anterior poliomyelitis, *July*, 35, 36
in treatment of anterior poliomyelitis, *July*, 41
pooled, in treatment of anterior poliomyelitis, *July*, 43
Copper poisoning in relation to hemochromatosis, *July*, 340
Cord, dressing, in newborn, *March*, 1418
Coronary occlusion, acute, without anginal pain, course, treatment and electrocardiographic findings, *Sept*, 477
differential diagnosis, difficulties from electrocardiographic standpoint, *July*, 219
oxygen therapy, *March*, 1488
thrombosis, *May*, 1510
complicating angina pectoris, *Nov*, 754
digitalis therapy, *May*, 1593
dissecting aneurysm of aorta and, differentiation, *Jan*, 1138
symptoms, *May*, 1511
treatment, *May*, 1512
Corpus luteum hormone, *Jan*, 1146, 1147, 1156
Corticomedullary portion of lymph gland, adenopathy affecting, *Nov*, 657
function, *Nov*, 638
Cough in myocardial failure in children, *May*, 1566
Creatine metabolism in Graves' disease, alterations in, *Nov*, 795
tolerance test in Graves' disease, *Nov*, 797
Crystallography of biliary drainage specimens, *July*, 171
Culture, blood, in acute fevers, technic, *Sept*, 573
of bile, *July*, 175
Curettage in menorrhagia and metrorrhagia, *Nov*, 786
Cutaneous See *Skin*
Cyanosis, pulmonary, *Sept*, 601
peripheral cyanosis and, differentiation, *Sept*, 601
Cyst, pancreatic, *March*, 1304, 1305
pulmonary, congenital, abscess of lung caused by, *Sept*, 441
Cyst, pulmonary, dermoid, abscess of lung caused by, *Sept*, 443
echinococcus, and pulmonary abscess, *Sept*, 444
Cytoplasm in transmission of diabetes, *July*, 273

Decubitus, angina of, *March*, 1272
Degenerative arthritis, *July*, 114, 118, *Jan* 947, 1014 See also *Arthritis, degenerative*
Delirium complicating pneumonia in children, treatment, *Nov*, 825
cordis, *July*, 343
Depression, agitated, following slight stroke, *Sept*, 543
De Rivas' transduodenal lavage for intestinal worms, *July*, 175
Dermatitis, allergic, *March*, 1253, 1254
medicamentosa, *March*, 1260
d'Espine sign in tuberculous thoracic glands, *Nov*, 650
Diabetes insipidus, *May*, 1597
chronic interstitial nephritis and differentiation, *May*, 1603
classification, *May* 1606
diagnosis, *May*, 1601
etiology, *May*, 1597
in children, *March*, 1461
posterior pituitary lobe, preparations for, *May*, 1604–1606
treatment, *May*, 1604
mellitus, complicating suprarenal tumor and hirsutism, *July*, 261
hereditary, *July*, 269
autosomes and, *July*, 273
cancer complicating, *July*, 276
clinical findings, *July*, 275
cytoplasm and, *July*, 273
differential diagnosis, 277
hemophilia complicating, *July*, 277
infection as factor in, *July*, 276
Mendelian law and, *July*, 271, 272
metabolic inferiority as factor, *July*, 281
obesity complicating, *July*, 275
potency and environment and, *July*, 274
predisposition to, *July*, 281
prophylaxis, *July*, 282
sex chromosomes and, *July*, 273
social and medical aspects, *Jan*, 1033
in infants and children, acidosis or alkalosis in, *Jan*, 1205
liberal carbohydrate diet in, *Nov*, 831

Diabetes mellitus, liberal carbohydrate diet in history of development Nov., 831
method and detail Nov 837
Diabetic coma with acidosis in children Jan 1224
regimen in hemochromatosis July 337
Diagnosis not made, July 329
Diaphragmatic paralysis in anterior poliomyelitis July 20
Diarrhea colonic irrigation in May 1615
complicating pneumonia in children treatment Nov 824
nervous Nov., 886
Diet carbohydrate liberal in diabetes mellitus Nov., 831
in acne vulgaris March 1469
in acute diffuse glomerular nephritis, March 1339
in acute nephritis Nov 868
in adiposogenital dystrophy July 251
in bronchial asthma of bacterial origin July 138
in chronic arthritis July 121
in chronic nephritis Nov 872
in gout March 1365
in mucous colitis Nov., 901
in nonspecific ulcerative colitis March 1372
in obesity Jan 1197 1200 1207
with amenorrhea Nov 781
in pneumonia in children Nov 815
in tuberculosis of skin July 325
in uremia Nov., 878
Digestive time table as aid in diagnosing gastric pain July 101 103
Digitalis history of May 1569
indications for use May 1583
physiological action May 1580
preparations of May 1589
therapy May 1579
electrocardiographic signs stimulating coronary occlusion July 222 229
in acute myocarditis May 1578
in auricular fibrillation July 315 Nov 749 May 1583
in auricular fibrillation and flutter May 1553 1583 1586
in cardiac hypertrophy Nov., 40 May 1591
in cardiovascular hypertensive disease May 1589
in chronic heart failure Nov 35
in congestive heart failure May 1583
Digitalis therapy in coronary thrombosis May 1593
in heart block, May 1586
in myocardial failure in children May 1561
in paroxysmal tachycardia May 1552 1597
in pericarditis with effusion May 1592
in pneumonia May 1591
in children Nov 821
in pulsus alternans May 1592
in various conditions May 1569
Dilatation of cervix for dysmenorrhea, March, 1279
Dinitrophenol in obesity Jan 1199
Disposition in children May 1668
Dissecting aneurysm of aorta. See Aneurysm
Distention gastric, pain in July, 94
Diuresis in auricular fibrillation July 350
Diuretics in myocardial failure in children May 1567
Diverticulitis Meckel's as surgical emergency July 13
Dorsal spine arthritis of Jan 960
physiotherapy in Jan 1027
Drainage biliary July 16
Drinker respirator in anterior poliomyelitis July 46
Dromedary cases in anterior poliomyelitis July 19
Drops nasal giving July 340 341
in acute sinusitis July 365 370
Duodenal drainage July 16
technic July 168
therapeutic value of July 174
ulcer chronic relation of to symptoms of visceroptosis postural correction for study of Nov 155
ulcer as cause of indigestion July 85
treatment July 87
gastric pain in July 98
perforation of as surgical emergency July 2
pneumonia and differentiation July 129
Duodenitis as cause of indigestion July 85
Dysentery amebic Nov 851
bacillary chronic May 1337
treatment May 1339
Dysmenorrhea Nov 7
dilatation of cervix for March 1279
due to endometriosis May 1250
to retroversion of uterus March 1281

Dysmenorrhea, hormone therapy, *Jan*, 1167, *March*, 1283
obstructive type, *March*, 1278
pessary treatment, *March*, 1281
specificity of cause and cure, *March*, 1282
treatment, *Nov*, 777
nonsurgical, *March*, 1277
Dyspnea, paroxysmal, in heart failure, treatment, *Nov*, 747
Dystrophia adiposogenitalis, *July*, 243
See also *Adiposogenital dystrophy*

EBURNATION, *July*, 114
Echinococcus cyst of lung and pulmonary abscess, *Sept*, 444
Eclampsia, new concept of, *July*, 297
prevention and control by fluid limitation and dehydration (Temple method), *July*, 297
treatment *July*, 297
of convulsive group, *July*, 302
of inherently normal group, *July*, 299
of moderately preeclamptic group, *July*, 301
of potentially abnormal group, *July*, 300
Ectopic pregnancy, rupture of, as surgical emergency, *July*, 69
Eczema, adenopathy secondary to, *Nov*, 644
atopic, *March*, 1253, 1254
of allergic origin, *March*, 1253
Edema in acute nephritis, treatment, *Nov*, 869
in chronic nephritis, treatment, *Nov*, 874
in myocardial failure in children, *May*, 1567
of pregnancy, treatment, *March*, 1501
pulmonary, oxygen therapy, *March*, 1488
Effort syndrome, treatment, *May*, 1548
Elbow joint, arthritis of, *Jan*, 9
physiotherapy in, *Jan*, 1020
Elbows, deformities in, prevention in arthritis, *Sept*, 554
Electrocardiographic diagnosis of coronary occlusion, difficulties in, *July*, 219
Elliott treatment of inflammatory disease of pelvis, *Sept* 473
Embolism, mesenteric, as surgical emergency, *July*, 77
Emetine in intestinal amebiasis, *Nov*, 854
Emmenin in adiposogenital dystrophy, *July*, 251
Empyema complicating pneumonia in children, treatment, *Nov*, 824
in infants and children, *Sept*, 454
Endocarditis, acute, treatment, *May*, 1515
bacterial, acute, treatment, *May*, 1516, 1517
subacute, treatment, *May*, 1521
lenta, treatment, *May*, 1521
rheumatic, acute, treatment, *May*, 1516
syphilitic, treatment, *May*, 1523
Endocervicitis, nongonorrheal, as cause of leukorrhea, *May*, 1701
Endocrine disorders in children with particular reference to treatment, *March*, 1443
dysfunctions, female, *Jan*, 1149
importance of history, *Jan*, 1149
of physical examination, *Jan*, 1153
treatment, *Jan*, 1157
therapy See *Hormone therapy*
Endocrinology female sex, *Jan*, 1143
See also *Hormone therapy*
Endometriosis dysmenorrhea due to, *March*, 1280
Endometrium, carcinoma of, as cause of leukorrhea, *May*, 1699
Environment and hereditary diabetes, *July*, 274
Ephedrine as shrinking agent in nasal passages, *July*, 368, 369
in orthostatic hypotension, *Sept*, 593
Epidural space spinal, abscess of, *July*, 287
Epigastric distress, recurring, differential diagnosis, *March* 1287
pain, *July*, 94
causes of *July* 101
tenderness, localized, causes of, *July*, 102
Epilepsy, possible, in overly ambitious Jewish young man, *Sept*, 544
Epitrochlear glands enlarged in syphilis, *Nov*, 655
Equine liver extract, subcutaneous use, in pernicious anemia, *Sept* 391
Ergot in pneumonia, *Sept*, 452
Erysipelas, antitoxin treatment, intramuscular method, *Nov*, 862
observations on 4698 patients, *Nov*, 861, 864
reasons for failure, *Nov*, 863
serum sickness in, *Nov*, 864

Erythema nodosum with Henoch's purpura hypersensitivity in *March* 1237
Erythrocytic sedimentation test application in special problems *Nov* 912
practical value, *Nov* 911
technic, *Nov* 912
Estrin *Jan.*, 1146
therapy in adiposogenital dystrophy *July* 249
Estrus cycle in mouse *Jan* 1150
Ewing's reticulum cell sarcoma of lymph nodes, *Nov* 668
Exercise in arthritis rules for *Sept* 564
in obesity *Jan* 1198
in chronic arthritis *July* 126
pelvic roll, *Jan* 985
Exophthalmic goiter See *Graves disease*
Exophthalmos, degree of variations in exophthalmic goiter *Nov* 793
Extralin in treatment of pernicious anemia *Sept* 385

FACIAL paralysis in anterior poliomyelitis, *July*, 21
Failing heart *Nov* 727
False aneurysm spontaneous of popliteal artery *Sept* 613
Fatigue in anterior poliomyelitis avoiding *July* 57
Favus, adenopathy secondary to *Nov* 641
Febrile albuminuria *March* 1334
diseases acute erythrocytic sedimentation test in value *Nov* 915
Feeding artificial of newborn *March* 1416
breast of newborn *March* 1413
supplemental of newborn *March* 1415
Feet deformities in prevention in arthritis *Sept* 561
Felty's syndrome *Jan* 1063
Female sex hormonology *Jan* 1143
Fever in anterior poliomyelitis, *July* 16
long-continued with inflammatory changes in serous and synovial membranes and eventual glomerulonephritis *Jan* 1073
Fevers acute blood cultures in technic, *Sept* 543
Fibrillation auricular See *Auricular fibrillation*
Fibroids of uterus pedunculated submucous as cause of leukorrhea *May* 1699
Finger joints arthritis of *Jan*, 955
physiotherapy in *Jan* 1019
Fingers deformities in prevention in arthritis *Sept* 556
Flatfeet in production of arthritis *Jan* 967
Flatulence in mucous colitis *Nov* 895
Foci of infection in chronic arthritis *July* 111
removal *July* 120
Follicular hormone *Jan* 1146 1147
dosage, *Jan* 1156
in treatment of adiposogenital dystrophy *July* 250
lymphoblastoma *Nov* 663 710
Folliculin *Jan* 1146
in treatment of adiposogenital dystrophy *July* 248
Fomites in transmission of anterior poliomyelitis *July* 33
Food residues in biliary drainage specimens, *July* 174
Foot joints, degenerative arthritis of *Jan* 966
strain *Jan* 983
Foreign body in lung *Sept* 456
Fowler's solution in chorea *Jan* 1088
Frei test in lymphogranuloma in guinale *Nov* 656
Fresh air in pneumonia in children *Nov* 815
Fruhlich's syndrome *July* 243 *Jan* 1194
endocrine therapy *March* 1452
Fusospirochetal infections *May* 1711
diagnosis *May* 1716
treatment *May* 1721

GALLBLADDER disease as cause of indigestion *July* 81
treatment *July* 84
in pernicious anemia *Jan.*, 939
pain *July* 100 105
perforation of as surgical emergency *July* 75
Galvanocautery in treatment of tuberculous laryngitis *March*, 1350
Gastric See *Stomach*
Gastritis chronic as cause of indigestion *July* 89
Gastro-enterologic practice insanity equivalents and actual or anxiety seen in *Sept* 541
Gastrointestinal diseases *Nov* 499
cardiac insufficiency associative *Sept* 491
disturbances in infancy and childhood acidosis and alkalosis in *Jan* 1205

Gastro intestinal symptoms from common duct stone, *Sept*, 500
in Addison's disease, *Sept*, 513
in gastrojejunal ulcer, *Sept*, 509
in peptic ulcer followed by carcinoma, *Sept*, 505
long standing, in pernicious anemia, *Jan*, 939
probably referable to goiter, *Sept*, 503
tract, atresia of, in newborn, *March*, 1408
hemorrhage from, in newborn, *March*, 1409
Gastrojejunal ulcer, gastro-intestinal symptoms, *Sept*, 509
Gaucher's disease, *Nov*, 686
German measles, adenopathy secondary to, *Nov*, 645
Gerson's diet in tuberculosis of skin, *July*, 325
Giardia in biliary drainage specimen, *July*, 173
Gibbus back, *Nov*, 651
Glandular fever in relation to status lymphaticus, *Nov*, 696
Pfeiffer's, *Nov*, 657
infectious mononucleosis and, differentiation, *Nov*, 669
Glomerulonephritis, acute diffuse, *March*, 1331
chronic, *Sept*, 403, 406
probable, tuberculous pleurisy with, *Sept*, 395
following long-continued fever with inflammatory changes in serous and synovial membranes, *Jan*, 1023
Glossopharyngeal paralysis in anterior poliomyelitis, *July*, 21
Glucose in bronchial asthma, *July*, 140
intravenously in eclampsia, *July*, 303
Glycogenesis and diabetes, *July*, 279
Glycogenolysis and diabetes, *July*, 279
Glycolysis and diabetes, *July*, 280
Goiter, exophthalmic See *Graves' disease*
with gastro-intestinal symptoms suggesting functional gastro-intestinal disease, *Sept*, 503
Goldthwait postural treatment in visceroptosis, *July*, 157, 158
Gonococcal arthritis, *Jan*, 991
Gout, *March*, 1355
alcohol addiction and, *Jan*, 1004
atrophic arthritis and, differentiation, *Jan*, 1009
complicated by gastric ulcer and anemia, *Jan*, 1053
Gout, diagnosis *Jan*, 999, *March*, 1364
familial tendency in, *Jan*, 1001
history, *Jan*, 1008
irregular, *Jan*, 1007
laboratory studies, *Jan*, 1011
pathogenesis, *March*, 1357
pathology, *March*, 1359
physical examination, *Jan*, 1009
predisposing causes, *March*, 1360
rheumatic fever and, differentiation, *Jan*, 1005
symptoms, *March*, 1361
tophi in, *Jan*, 1010
treatments, *March*, 1365
type of person affected by, *Jan*, 1007
vascular disease complicating, *Jan*, 1010
Granules, sulphur, *May*, 1738
Granuloma, Hodgkin's, *Nov*, 673
Graves' constitution, *Nov*, 795
disease, alteration in quality of thyroid secretion in, *Nov*, 794
case reports, *Nov*, 799
common features with hypothyroid states *Nov*, 792
creatine metabolism in, alterations in, *Nov*, 795
tolerance test, *Nov*, 797
iodine in, *Nov*, 806
"escape" from, *Nov*, 806
pathology, *Nov*, 791
postoperative, symptoms and treatment, *Nov*, 807
relation of thyroid gland to, *Nov* 791
variations in degree of exophthalmos in, *Nov*, 793
Growing pains, *March*, 1473
Gummata, scrofulous, *July*, 319

Hay fever, *March*, 1235, 1245
asthma in, *Jan*, 996
Headache bilious See *Migraine*
in anterior poliomyelitis, *July*, 17, 19
Heart, adiposity of, *Sept*, 471
block, partial and complete, digitalis therapy, *May*, 1586
treatment, *May*, 1557
damaged, patient's mode of living at different periods of life, *Jan*, 1175
disease, complicating thyroid disease, two cases, *Jan*, 1027
congenital, in newborn, *March*, 1408
hypertensive, *Nov* 744
treatment, *Nov*, 746
jaundice in, *Sept*, 492

Heart disease, rheumatic, heart failure accompanying, *Nov.*, 742
  in children, convalescent care, *March* 1471; *May* 1569
    management, *Jan.*, 1067; *May* 1559
    myocardial failure complicating, *May* 1564, 1570
    with active rheumatic infection, *Jan.* 1071; *May* 1559
      and congestive failure, *Jan.* 1074
      and pericarditis with congestive failure, *Jan.* 1077
    without evidence of rheumatic infection, *Jan.* 1068; *May* 1577
  valvular, chronic, *Nov.* 744
    treatment, *Nov.* 746
  with involvement of both mitral and pulmonic valves, *July* 233
  with subarachnoid hemorrhage, *July* 307
  syphilitic, with bundle branch block, sino-auricular block and ventricular escapes in vagus overactivity of sinus node demonstrated, *March* 1383
failure, *Nov.*, 727
  acute, *Nov.* 729
    in mitral stenosis, hemoptysis as symptom, *Nov.* 917
    symptoms, *Nov.* 729
    treatment, *Nov.* 733
  chronic, *Nov.* 729
    digitalis in, *Nov.*, 735
    physiotherapy in, *Nov.* 737
    purgatives, laxatives, diuretics, sedatives, vasodilators in, *Nov.* 737, 738
    rest in, *Nov.* 73
    symptoms, *Nov.* 730
    treatment, *Nov.* 735
  complicating rheumatic heart disease, *Nov.* 743
  congestive, digitalis therapy, *May* 1583
    electrocardiographic signs simulating coronary occlusion, *July* 227, 228
    in rheumatic heart disease in children, *May* 1561, 1570
    syphilitic, *May* 153
  diagnosis, *Nov.* 732
  due to overexertion, treatment, *Nov.* 748
  early treatment, *Nov.*, 741
Heart failure, etiology, *Nov.*, 727
  in hypertrophy of heart, *Nov.* 744
    treatment, *Nov.* 746; *May* 1594
  manifested by anginal pain, *Nov.* 753
    treatment, *Nov.*, 753
  nocturnal asthma in, treatment, *Nov.* 747
  paroxysmal dyspnea in, treatment, *Nov.* 747
  pathology, *Nov.* 729
  recognition and management, *Nov.* 727
  in rheumatic fever and acute rheumatoid (infectious) arthritis, *Nov.* 759
  inflammation of, acute, treatment, *May* 1515
  insufficiency, oxygen therapy, *March* 1488
    symptoms masked by those referable to gastro-intestinal tract, *Sept.* 491
  irregularity of, treatment, *May* 1515
  syphilis of, treatment, *May* 1533
    neoarsphenamine technic and results, *May* 1531, 1536, 1538
    reactions to arsphenamine, *May* 1533
  tamponade, *May* 1514
Heberden's nodes, *Jan.* 955; *July* 114
Hematopoietic disease, adenopathy secondary to, *Nov.* 691
Hemochromatosis, *July* 337
  copper poisoning in relation to, *July* 310
  diabetic regimen in, case illustrating, *July* 33
  pathogenesis, *July* 310
Hemophilia complicating hereditary diabetes, *July* 2
  in production of degenerative arthritis, *Jan.* 952
Hemoptysis as symptom of acute heart failure in presence of mitral stenosis, *Nov.* 917
Hemorrhage, cerebral, in newborn, *March* 1401
  from gastro-intestinal tract in newborn, *March* 1409
  subarachnoid, complicating rheumatic heart disease, *July* 30
Henoch purpura with erythema multiforme hypersensitivity in, *March* 123
Hepatointestinal [illegible] drainage in, [illegible]

Hereditary diabetes, *July*, 269
social and medical aspects, *Jan*, 1033
gout, *Jan*, 1001
Hernia, Richter's, as surgical emergency, *July*, 76
umbilical, in newborn, *March*, 1409
Herrmannsdorfer's diet in tuberculosis of skin, *July*, 325
Hip, deformities in, prevention in arthritis, *Sept*, 560
joint, arthritis of, *Jan*, 962
physiotherapy in, *Jan*, 1019
Hirsutism complicating suprarenal tumor and diabetes, *July*, 261
unusual case, *Sept*, 411
Hodgkin's disease, *Nov*, 673, 714
aneurysm of aorta and, differentiation, *Nov*, 678
blood picture in, *Nov*, 682
diagnosis, *July*, 188
etiology, *Nov*, 674
intra abdominal *Nov*, 679
intrathoracic, *Nov*, 678
irradiation in, *Nov*, 715
mediastinal type, *July*, 177
mode of distribution of affected glands, *Nov*, 673
nomenclature, *July*, 188
pathology, *Nov* 675
prognosis, *Nov* 684
symptomatology, *Nov*, 677
thyroid tumor and, differentiation, *Nov* 678
treatment, *Nov*, 684, 714
lymphogranuloma, *Nov*, 673
Hormone, corpus luteum, *Jan*, 1146, 1147, 1156
follicular, *Jan*, 1146, 1147
dosage, *Jan*, *1156*
therapy, clinical significance and applications, *Jan*, 1149
dosage, *Jan*, 1155
importance of history, *Jan*, 1149
of physical examination, *Jan*, *1153*
in amenorrhea, *Nov*, 782, 788
Jan, 1157
in dysmenorrhea, *Jan*, *1167*
March, 1283
in endocrine disorders in children, *March*, 1443
in menopause *Jan* 1170
in menorrhagia and metrorrhagia, *Nov*, 788 *Jan*, 1161
in menstrual disorders, *Nov*, 788, *Jan*, 1157
in oligomenorrhea, *Nov*, 782
Jan, 1157
Hormones, female, *Jan*, 1144
Hormones, female, action of, *Jan*, 1146
clinical significance and applications, *Jan*, 1149
interrelationships, *Jan*, 1149
laboratory tests, *Jan*, 1147
pathology, *Jan*, 1148
Hormonology, female sex, *Jan*, 1143
Hydrotherapy in chronic heart failure, *Nov*, *737*
Hygiene of newborn infant, *March*, 1417
Hyperesthetic rhinitis, *March*, 1245
radium treatment, *March* 1250
Hyperirritable colon, *Nov*, 887
Hyperparathyroidism, *Jan*, 1109
case with unusual features, *Jan*, 1109
electrocardiographic signs simulating coronary occlusion, *July*, 227
Hypersensitivity See also *Allergic diseases*
in diseases of skin, *March*, 1253
in Henoch's purpura with erythema nodosum, *March*, 1237
in rheumatic disease, *March*, 1237, *1240*
to ingesta in migraine, *March*, 1241
Hypertension, electrocardiographic simulation of coronary occlusion, *July*, 222, 224
in nephritis, treatment, *Nov* 876
malignant, early, sympathectomy for, *Sept*, 577
Hypertensive disease, cardiovascular, digitalis therapy, *May*, 1589
heart disease, *Nov*, 744
treatment, *Nov*, 746
Hyperthyroidism with gastro-intestinal symptoms suggesting functional gastro intestinal disease, *Sept*, 503
Hypertonic solutions in eclampsia, *July*, 303, 304
Hypertrophic arthritis See *Arthritis, degenerative*
heart, failure of, *Nov*, 744
digitalis therapy, *Nov*, 744
May, 1594
Hypoglossus paralysis in anterior *poliomyelitis*, *July*, 21
Hypoglycemia of pregnancy, treatment *March*, 1495
Hypophysis See *Pituitary*
Hypopituitarism, anterior lobe, *July*, 252
in young child, *March*, 1460
juvenile, in female, *March*, 1455
in male, *March* 1452

Hypotension orthostatic (postural) with syncope *Sept* 585
treatment *Sept* 591
Hypothyroidism juvenile thyroid treatment *March* 1443

Icterus neonatorum *March* 1413
Idiosyncrasy See *Allergic diseases*
Ileus paralytic and mechanical roentgen differentiation *March* 1432
Immobilization in anterior poliomyelitis *July* 45 55
Immune serum in puerperal sepsis *March* 1395
Impetigo in newborn *March* 1412 1418
Indigestion causes of analysis of 212 cases *July* 81
diagnosis and treatment *July* 81
in appendicitis *July* 90
in carcinoma of stomach *July* 89
in chronic gastritis *July* 89
in duodenal ulcer *July* 85 86
in duodenitis *July* 87
in functional disturbances of colon *July* 87 88
of stomach *July* 87 88
in gallbladder disease *July* 84
long standing in pernicious anemia *Jan* 939
Infantile paralysis. See *Poliomyelitis anterior*
Infants acidosis or alkalosis in *Jan* 1205
newborn *March* 1403 See also *Newborn infant*
pneumonia in treatment *Nov* 811
Infarction of lung abscess secondary to *Sept* 435
Infections, abdominal acute as surgical emergencies *July* 73
as factor in hereditary diabetes *July* 276
local adenopathy secondary to *Nov* 642
of newborn *March* 1411
systemic, adenopathy secondary to *Nov* 614
visceral evidences of *July* 141
Infectious arthritis rheumatic fever and differentiation *Nov* 759
mononucleosis *Nov* 669 696 713
Inflammation of heart acute treatment *May* 1515
Inflammatory changes in synovial and serous membranes with long continued fever and eventual glomerulonephritis *Jan* 1033
Inflammatory disease of pelvis Elliott treatment *Sept* 423
Inguinal glands syphilis of *Nov* 654
tuberculous *Nov* 648
Injuries abdominal roentgen diagnosis *March* 1431
birth *March* 1404
Insanity equivalents and actual in sanity seen in gastro-enterologic practice *Sept* 541
Insects in transmission of anterior poliomyelitis *July* 33
Intellectually inferior children *May* 1665
Intercostal neuritis *Jan* 981
paralysis in anterior poliomyelitis *July* 20
Intermedin *July* 741
in diabetes insipidus *May* 1606
Intermittent claudication effect of tissue extracts on *Sept* 609
Intestinal amebiasis See *Amebiasis*
atony colonic irrigations in *May* 1614 1619
diseases *Sept* 535
obstruction as surgical emergency *July* 76
roentgen diagnosis *March* 1429
toxemia in mucous colitis *Nov* 896
with constipation colonic irrigations in *May* 1615 1619
worms transduodenal lavage for *July* 1 5
Intra abdominal glands tuberculous *Nov* 651
Hodgkin's disease *Nov* 619
lymphosarcoma *Nov* 665
Intracutaneous tests in allergic diseases *March* 1230
Intradermal reactions to determine presence of visceral infection *July* 145
Intranasal lupus treatment *July* 324
Intussusception as surgical emergency *July* 76
of sigmoid due to malignant polyp *Sept* 539
roentgen diagnosis *March* 1430
Iodine in Graves disease *Nov* 809
escape from *Nov* 809
Iodobismuthquinoline in intestinal amebiasis *Nov* 855
Iron deficiency anemia in inoperable carcinoma of stomach treatment *Jan* 1183
Irradiation See *Radium* and *Roentgen*
Irrigation colonic *May* 1611
in chronic arthritis *July* 134

Irritability in man with bad nervous heredity, *Sept*, 544
Irritable colon, *Nov*, 887

JAUNDICE in myocardial insufficiency, *Sept*, 492
in newborn, *March*, 1413
Jaws, deformities in, prevention in arthritis, *Sept*, 550
Joint changes in chronic arthritis, *July*, 112, 114
pain, defective posture as cause, *Jan*, 976
importance of mechanical trauma in, *Jan*, 971
in rheumatic heart disease in children, *May*, 1560
strain, static and postural defects as cause, *Jan*, 976–980
Joints Charcot, *Jan*, 951
incorrect use, effect of, *Jan*, 975
painful, with splenomegaly and anemia, three cases, *Jan*, 1053

KIDNEY disease clinical problems in management, *Sept*, 395
insufficiency, chronic, severe, with acidosis in childhood, *Jan*, 1220
rupture of, as surgical emergency, *July*, 68
King's evil, *July*, 319
Knee joint, arthritis of, *Jan*, 964
physiotherapy in, *Jan*, 1016
prevention of deformities, *Sept*, 560
strain, *Jan*, 983
Kussmaul breathing in acidosis, *Jan*, 1209

LACERATIONS of cervix, leukorrhea due to, *May*, 1701
Laguere sign in sacro iliac disease, *Jan*, 962
Lamblia intestinalis in biliary drainage specimens, *July*, 173
Laryngitis, hyperplastic, tuberculous laryngitis and, differentiation, *March*, 1379
tuberculous, progressive, diagnosis and treatment, *March*, 1377
Larynx, carcinoma of, tuberculosis of larynx and, differentiation, *March*, 1378
syphilis of, tuberculosis of larynx and, differentiation, *March*, 1378
Lavage, transduodenal, for intestinal worms, *July*, 175
Legs, thrombophlebitis of, recurrent idiopathic, *Sept*, 597
Leucine crystals in biliary drainage specimens, *July*, 171
Leukemia, lymphatic, *Nov*, 658
acute, *Nov*, 658
chronic, *Nov*, 659
treatment, *Nov*, 706
subleukemic, thrombocytopenia and, differentiation, *Nov*, 659
monocytic, *Nov*, 672
myelogenous, *Nov*, 691
arsenic in, *Nov*, 723
irradiation in, *Nov*, 721
treatment, *Nov*, 720
Leukorrhea, clinical significance and treatment, *May*, 1697
mucopurulent, *May*, 1701
Leukosarcoma *Nov*, 684
Lipiodol insufflation in bronchiectasis, *Jan*, 1044
Liver and stomach preparation (extralin) in pernicious anemia, *Sept*, 385
diseases of, epigastric distress in, *March*, 1289
equine, extract of, subcutaneously in pernicious anemia, *Sept*, 391
rupture of, as surgical emergency, *July*, 66
Lobar pneumonia, oxygen therapy, *March*, 1487
Lobectomy in bronchiectasis, *Jan*, 1047
Lorain Levi disease, *July*, 252
Lotio alba in acne vulgaris, *March*, 1466
Luetic lymph glands, *Nov*, 654
Lumbago, *Jan*, 980
Lumbar spine, arthritis of, *Jan*, 960
physiotherapy in, *Jan*, 1022
prevention of deformities, *Sept*, 559
sacro iliac strain and, differentiation, *Jan*, 962
Lumbosacral strain, *Jan*, 981
Lung, abscess of, *Sept*, 429
aspiratory type *Sept*, 430
associated with acute pneumonia, *Sept*, 433
caused by possible dermoid cyst, *Sept*, 443
by single congenital pulmonary cyst, *Sept*, 441
complicating pneumonia in children, treatment, *Nov*, 825
echinococcus cyst and, *Sept*, 444
etiology, *Sept*, 429
metastatic, *Sept* 437

Lung abscess of secondary to infarction of lung *Sept* 435
to malignant disease of lung *Sept* 449
tuberculous *Sept* 448
actinomycosis of *May* 1725
case report *May* 1725
diagnosis, *May* 1738
historical résumé *May* 1736
incidence *May* 1737
prognosis and treatment *May* 1740
cyst of, congenital pulmonary abscess caused by *Sept.*, 441
dermoid abscess of lung caused by *Sept.*, 443
diseases of in infants and children *Sept* 451
edema of oxygen therapy *March* 1488
efficiency of vital capacity as test of present status, *May* 1685
infarction of abscess secondary to *Sept* 435
malignant disease abscess secondary to *Sept* 449
peanut in *Sept* 456
tuberculosis of erythrocytic sedimentation test in value *Nov* 914
unusual types *Sept* 459
Vincent's infection of *May* 1714
Lupus infectionis granulomata *July* 312
intranasal treatment *July* 324
of mucous membranes *July* 31[illegible]
treatment *July* 324
vorax, 312
verrucosus *July* 321
vulgaris *July* 312
treatment *July* 323 324
Luteo-hormon *Jan* 1146, 1156
Lymph circulation of *Nov* 634
glands *Nov* 634
anatomy and physiology of *Nov* 634
corticomedullary portion adenopathy affecting *Nov* 657
functions of *Nov* 638
diseases of *Nov* 633
enlarged See *Adenopathy* and *Lymphadenopathy*
in chancroid, *Nov* 655
intra-abdominal tuberculosis of *Nov* 651
luetic *Nov* 654
regional distribution *Nov* 636
reticulo-endothelium of adenopathy originating primarily in *Nov* 669
Lymph glands reticulo-endothelium of functions, *Nov* 639
superficial tuberculosis of *Nov* 648
thoracic tuberculosis of *Nov* 649
nodes *Nov* 634
Ewing's reticulum cell sarcoma of *Nov* 668
nodules *Nov* 634
vessels *Nov* 634
Lymphadenitis primary infectious of mesenteric glands *Nov* 647
tuberculous treatment *Nov* 705
Lymphadenoma generalized *Nov* 673
Lymphadenopathies treatment, with special reference to irradiation *Nov* 703
Lymphadenopathy carcinomatous treatment *Nov* 718
clinical interpretation *Nov* 633
mediastinal in tuberculous pericarditis *July* 210
Lymphatic leukemia *Nov* 658 See also *Leukemia lymphatic*
system anatomy and physiology *Nov* 634
Lymphoblastoma *Nov* 663
follicular *Nov* 663 710
Lymphocytosis in relation to status lymphaticus *Nov* 696
Lymphogranuloma Hodgkin's *Nov* 714
inguinale, *Nov* 656
Frei test in *Nov* 656
Lymphoma tuberculous diffuse *Nov.*, 657
Lymphosarcoma *Nov* 664
intra abdominal *Nov* 665
mediastinal *Nov* 665
responsiveness to x rays *Nov* 665
treatment *Nov* 711
vaginal *Nov* 664

Malignant disease of lung abscess secondary to *Sept* 449
hypertension early sympathectomy for *Sept* 574
Malum coxitis senilis *Jan* 962
Mandl Dallos disease *Jan* 1109
Manipulation in chronic infectious arthritis *Sept* 569
Massage in anterior poliomyelitis *July* 5
in chronic arthritis *Jan* 1[illegible]
in obesity *Jan* 1109
Mechanical and paralytic ileus treatment differentiation *March* 1432
therapeutics of anterior poliomyelitis *July* 51

Mechanical trauma, importance in joint pain, *Jan*, 971
Meckel's diverticulitis as surgical emergency, *July* 75
Mediastinal lymphadenopathy in tuberculous pericarditis, *July*, 210
lymphosarcoma, *Nov*, 665
type of Hodgkin's disease, *July*, 177
Melancholia seen in gastroenterological practice, *Sept*, 545
Mendelian law and hereditary diabetes, *July*, 271, 272
Menformon, *Jan*, 1146
Meningococcemia in infant with spontaneous recovery, *Sept*, 573
Meningeal irritation in anterior poliomyelitis, *July*, 18
conditions simulating, *July*, 24
Meningismus anterior poliomyelitis and, differentiation, *July*, 24
Menopause, hormone therapy at, *Jan*, 1170
leukorrhea following, *May*, 1707
Menorrhagia *Nov*, 773
causes, *Nov*, 772, 775
curettage in *Nov* 786
diagnosis, *Nov*, 775
endocrine therapy, *Nov*, 788 *Jan*, 1161
radiotherapeutic sterilization in *Nov* 786
treatment *Nov*, 783
Menstrual disorders *Nov*, 771
classification *Nov*, 771
diagnosis, *Nov* 773
endocrine therapy *Nov*, 788 *Jan* 1143
functional *Nov*, 772
due to pituitary derangements *July*, 239, 242
organic, *Nov*, 791
pelvic examination in *Nov* 773
pain, nonsurgical treatment, *March* 1277
Mesenteric glands acute tuberculosis of in children *Nov*, 652
primary infectious lymphadenitis of, *Nov*, 647
thrombosis and embolism as surgical emergency *July*, 77
Mesentery, rupture of, as surgical emergency *July*, 69
Metabolic disturbances causing splenic enlargement, *Nov* 686
inferiority in hereditary diabetes, *July*, 281
Metacarpophalangeal articulations arthritis of, physiotherapy in, *Jan*, 1018
Metropathia hemorrhagica of Schröder, *Jan*, 1161
Metrorrhagia, *Nov*, 773
causes, *Nov*, 772, 775
curettage in *Nov*, 786
diagnosis, *Nov*, 775
endocrine therapy, *Jan*, 1161
treatment, *Nov*, 783
Microscopy of biliary drainage specimens *July*, 171
Migraine, *Nov*, 827
hypersensitivity to ingestain, *March*, 1240
pathogenesis, *Nov*, 827
treatment, *Nov*, 827
Mikulicz disease *Nov* 684
Miliary tuberculosis, *July*, 322
Milk, breast, for newborn, *March*, 1413
supplies and anterior poliomyelitis, *July*, 32
Mitral stenosis, acute heart failure in, hemoptysis as symptom, *Nov* 917
valvulitis with pulmonic involvement in rheumatic heart disease *July*, 233
Moccasin venom in puberty bleeding, *Nov*, 784
Moncrieff's treatment of cerebral hemorrhage in newborn, *March*, 1405
Monilia infections of vagina, *May* 1710
Monocytic leukemia *Nov* 672
Mononucleosis infectious, *Nov* 669, 713
in relation to status lymphaticus *Nov*, 696
Paul Bunnell test in, *Nov* 670, 713
Pfeiffer's glandular fever and, differentiation *Nov*, 669
treatment *Nov* 713
Morning paralysis in anterior poliomyelitis *July* 15
Mouth, trench, *May* 1712
Mucopurulent leukorrhea, *May*, 1701
Mucous colitis See *Colitis, mucous*
membranes lupus of, *July*, 317
treatment *July* 324
Mucus, shaggy in biliary drainage, *July* 173
Muscle equilibrium in earliest stage of poliomyelitis *July* 54
reeducation in anterior poliomyelitis, *July*, 58
relaxation after beginning of paralysis in poliomyelitis, *July*, 56

Mycosis fungoides treatment *Nov* 711
Myelogenous leukemia *Nov* 691
  treatment, *Nov* 720
Myocardial failure complicating rheumatic heart disease in children *May* 1564, 1570
  insufficiency jaundice in *Sept.*, 492
Myocarditis, acute treatment *May* 1526
Myosten effects of on intermittent claudication *Sept* 610 612
Myxedema juvenile thyroid treatment *March* 1443

NASAL disease allergic, *March* 1233 1235 1245
  radium treatment *March* 1250
  drops giving *July* 340
  in acute sinusitis *July* 368 340
Nausea in acute appendicitis *March* 1490
Neck, deformities in prevention in arthritis, *Sept* 551
  lymph glands of syphilitic, *Nov* 654
    tuberculous *Nov* 618
  reflex, Brudzinski's in anterior poliomyelitis *July* 26
Neckache *Jan* 980
Neoarsphenamine in treatment of syphilis of heart *May* 1534
  in Vincent's disease *May* 1721 1722 1723
Nephritis, acute *Nov* 868
    anuria in treatment *Nov* 870
    diet in *Nov* 868
    diffuse glomerular *March* 1331
      stage of transition *March* 1335
      treatment *March* 1338
    edema in treatment *Nov* 869
    general management *Nov* 868
    medicinal treatment *Nov* 871
    physiotherapy in *Nov* 871
    surgery in *Nov* 871
  chronic *Nov* 872
    anemia in treatment *Nov* 876
    cardiac complications in treatment *Nov* 876
    diet in *Nov* 872
    effects of dietary protein salt and water intake on edema *Nov* 874
    general management *Nov.*, 873
    hypertension in treatment *Nov* 876
    in infants and children acidosis or alkalosis in *Jan* 1305
Nephritis chronic interstitial diabetes insipidus and differentiation *May* 1603
    medicinal treatment *Nov* 875
    physiotherapy in *Nov* 877
    surgery in *Nov* 877
Nervous diarrhea *Nov* 886
    manifestations in mucous colitis *Nov* 891
      treatment *Nov* 907
    regurgitation *Sept* 516
Neufeld typing in pneumonia *Jan* 1091
Neuritis intercostal *Jan* 981
Neuropathic constitution in children *May* 1666
Neuroses value of erythrocytic sedimentation test in *Nov* 912
Neutralization test in poliomyelitis in study of immunity *July* 7
Neutropenia in relation to status lymphaticus, *Nov* 69
Newborn infant *March* 1403
    asphyxia in *March* 1404
    birth injuries *March* 1401
    caput succedaneum in *March* 1408
    cerebral hemorrhage in *March* 1404
    clothing of *March* 1418
    congenital abnormalities *March* 1408
    dressing cord *March* 1418
    feeding artificial *March* 1416
      breast *March* 1413
      supplemental *March* 1415
    hygiene of general *March* 1417
    impetigo in *March*, 1418
    infections of *March* 1411
    nutrition of *March* 1413
    physiologic changes in *March* 1417
    prophylaxis *March* 1419
    syphilis in *March* 1411
    thrush in *March* 1419
    weight loss, physiologic *March* 1415
Niemann Pick's disease *Nov* 688
Nirvanol in chorea *Jan* 1089
Nocturnal asthma in heart failure treatment *Nov* 4
Nodes Heberden's *July* 112 *Jan* 955
Nucleus paraventricularis *May* 1598 1600
    supraopticus *May* 1598 1600
Nutrition of newborn *March* 1413
Nutritional disturbance acute with dehydration and acidosis in infant *Jan.*, 1214

Obesity, *Jan*, 1191
complicating hereditary diabetes, *July*, 275
diet in, *Jan*, 1197, 1200, 1202
drugs in, *Jan*, 1199
endogenous, *Jan*, 1194
etiology, *Jan*, 1191
exercise in, *Jan*, 1198
exogenous, *Jan*, 1192
massage in, *Jan*, 1199
pituitary, *Jan*, 1194
juvenile, *March*, 1452, 1455
treatment, *Jan*, 1196
prolonged, *Jan*, 1200
with amenorrhea, treatment, *Nov*, 780
Obstruction, intestinal See *Intestinal obstruction*
Occupation, degenerative arthritis and, *Jan*, 949
Occupational therapy for cardiac children, *March*, 1476
Oculomotor paralysis in anterior poliomyelitis, *July*, 21
Oligomenorrhea, *Nov*, 772
endocrine therapy, *Jan*, 1157
treatment, *Nov*, 779
Ophthalmia neonatorum, prevention, *March*, 1419
Orthopedic nonsurgical treatment of anterior poliomyelitis, *July*, 51
Orthostatic hypotension with syncope, *Sept*, 585
treatment, *Sept*, 591
Osteo arthritis See *Arthritis, degenerative*
Otitis media in pneumonia in children, treatment, *Nov*, 824
Ovarian overfunction, *Nov*, 772
treatment, *Nov*, 783 *Jan*, 1161
underfunction, *Nov*, 772
treatment, *Nov*, 779, *Jan*, 1157
Ovary, pituitary control of, *July*, 241
tumors of, in children, *March*, 1462
Overexertion as exciting cause of coronary thrombosis, *Nov*, 754
heart failure due to, treatment, *Nov*, 748
Oxygen therapy in home, *March*, 1485
apparatus for, *March*, 1486
indications for, *March*, 1485
kinds to use, *March*, 1483
method of administration, *March*, 1487
in myocardial failure in children, *May*, 1568
in pneumonia in children, *Nov*, 818
Oxyquinoline in intestinal amebiasis, *Nov*, 856
Oxytocin, *July*, 240

Pain, abdominal, in mucous colitis, *Nov*, 894
roentgen diagnosis of extra abdominal lesions causing, *March*, 1439
anginal, heart failure manifested by, *Nov*, 753
treatment, *Nov*, 755
epigastric, *July*, 94
causes of, *July*, 101
recurring, differential diagnosis, *March*, 1287
gallbladder, *July*, 100, 105
gastric, *July*, 93 See also *Stomach, pain in*
growing, *March*, 1473
in acute appendicitis, *March*, 1489
in pancreatic disease, *July*, 100
in perisplenitis, *July*, 100
in splenic disease, *July*, 100
in thrombo angiitis obliterans, common types, *Sept*, 623
joint See *Joint pain*
menstrual, nonsurgical treatment, *March*, 1277
of angina pectoris, *May*, 1507
of coronary thrombosis, *May*, 1511
of peptic ulcer, *March* 1288
of three years' duration preceding operation for bronchiectasis, *Jan*, 1049
Pancreas, body and tail, carcinoma of, *March*, 1306
carcinoma of, *March*, 1298
carcinoma of, symptoms, *March*, 1312, 1315
cysts of, *March*, 1304, 1305
diseases of, symptoms and mechanism of their production, *March*, 1289
head, carcinoma of, *March*, 1311
tail, carcinoma of, with carcinomatosis of peritoneum and omentum, *March*, 1309
Pancreatic disease, pain in, *July*, 100
tissue extract, effects of, on intermittent claudication, *Sept*, 611, 612
Pancreatitis, *March*, 1302
acute, as surgical emergency, *July*, 77
chronic, complicating pernicious anemia, *Sept*, 520
sprue and, differential diagnosis, *Sept*, 526

Pancreatitis chronic steatorrhea and azotorrhea in diagnostic value *Sept* 519
symptoms *March* 1316
with cyst in body of pancreas, *March* 1304
in head of pancreas *March* 1305
Pannus formation in atrophic arthritis *July* 112
Paracentesis of pericardium *May* 1525
Paralysis, infantile See *Poliomyelitis anterior*
Paralytic and mechanical ileus roentgen differentiation *March* 1432
Paranoid reaction type, *July* 353
Parasites in biliary drainage specimens *July* 173
Parathyroid tissue hyperplasia of in hyperparathyroidism *Jan* 1109
Parous cervix as source of leukorrhea *May* 1601
Paroxysmal dyspnea in heart failure treatment *Nov* 681
tachycardia digitalis therapy *May* 1582 1592
treatment *Nov* 752 *May* 1549 1551
Patch test in allergic diseases *March* 1231 1251
Paul Bunnell test in infectious mononucleosis *Nov* 610 713
Peanut in lung *Sept* 456
Pediatrician problems of See under *Children*
Pelvic backache *Jan* 982
examination in menstrual disorders *Nov*, 773
roll exercise *Jan* 985
Pelvis inflammatory disease of Elliott treatment *Sept* 423
Pemphigus syphilitica in newborn *March* 1412
Peptic ulcer as cause of indigestion *July* 85 86
carcinoma developing in *Sept* 505
complicating gout *Jan* 1053
gastric pain in *July* 95
pain of *March* 1288
perforation of as surgical emergency *July* 73
pneumonia and differentiation *July* 199
roentgen diagnosis, *March* 1423
syndrome of atypical *March* 178
Perforation of appendiceal abscess *July* 73
of duodenal ulcer *July* 82
Perforation of gallbladder *July* 78
of peptic ulcer *July* 73
pneumonia and differentiation *July* 199
roentgen diagnosis *March* 1423
of typhoid ulcer *July* 73
Pericarditis acute treatment *May* 1524
adhesive tuberculous origin *July* 209
diagnosis *July* 216
diagnosis *July* 212
rheumatic tuberculous pericarditis and differentiation *July* 215 216
tuberculous *July* 201
clinical and pathologic study based on 17 cases *July* 201
diagnosis *July* 212
incidence *July* 205
in relation to age sex, and race *July* 205
mediastinal lymphadenopathy in *July* 210
other tuberculous pathology accompanying *July* 210
pathology *July* 206
primary *July*, 210
rheumatic pericarditis and differentiation *July* 215 216
source of infection *July* 206
stages of *July* 208
symptomatology *July* 211
with effusion digitalis therapy *May* 1592
tuberculous origin *July* 208
recognition of *July* 214
Pericardium paracentesis of *May* 1525
Peripheral cyanosis pulmonary cyanosis and differentiation *Sept* 601
Perisplenitis, pain in *July* 100
Pernicious anemia See *Anemia pernicious*
Pessaries, use of in dysmenorrhea due to retroversion *March* 1281
Pfannenstiel's treatment of intranasal lupus, *July* 324
Pharyngeal paralysis in anterior poliomyelitis treatment *July* 47
Pharyngitis ulcerative *May* 1711
Pfeiffer's glandular fever *Nov* 657
infectious mononucleosis and differentiation *Nov*, 669
Phototherapy in cutaneous tuberculosis, *July* 373
Physiologic changes in neonatum *March* 1412
low of weight in newborn *March*, 1415

Physiologic rest in anterior poliomyelitis, *July*, 54
Physiotherapy for cardiac children, *March*, 1476
in arthritis, *July*, 125, *Jan*, 1013, 1015
in chronic heart failure, *Nov*, 737
Pigment metabolism, excessive, in pernicious anemia, *Jan*, 941
Pimples, *March*, 1465
Pinealism in children, *March*, 1462
Pitocin, *July*, 240
Pitressin, *July*, 240
Pituitary adenoma, acidophilic, *July*, 255
basophilic, *July*, 256
chromophobe, *July*, 254
basophilism with suprarenocortical syndrome, *Sept*, 411
cachexia, *July*, 253
extract, anterior, in obesity, *Jan*, 1199
gland, anatomy, *July*, 240
control of ovary by, *July*, 241
derangements, functional, menstrual disorders due to, *July*, 239, 242
physiology, *July*, 240
obesity, *Jan*, 1194
juvenile, *March*, 1452, 1455
therapy in adiposogenital dystrophy, *July*, 247
in anterior lobe hypopituitarism, *July*, 252
Pituitrin, *July*, 240
in diabetes insipidus, *May*, 1604, 1605
Placental tissue, retained, as cause of leukorrhea, *May*, 1698
Plasma, normal, composition of, *Jan*, 1206
Pleurisy, tuberculous, with probable chronic glomerulonephritis, *Sept*, 395
Plugging of bronchus in pneumonia in children, treatment, *Nov*, 825
Pluriglandular syndrome associated with carcinoma of right suprarenal gland, *March*, 1367
Pneumococcus pneumonia, diagnosis, *Jan*, 1096
types in pneumonia, and serum treatment, *Jan*, 1094
Pneumonia, acute, abscess of lung associated with, *Sept*, 433
appendicitis and, differentiation, *July*, 200
bronchial See *Bronchopneumonia*
cholecystitis and, differentiation, *July*, 200
Pneumonia, digitalis therapy, *May*, 1591
following whooping cough, *Sept*, 455
in infants and children, *Sept*, 451, *Nov*, 811
complications and their treatment, *Nov*, 824
convalescence, *Nov*, 825
diet and fluid needs, *Nov*, 815
digitalis medication, *Nov*, 821
drugs in, *Nov*, 819
epidemic nature of, *Nov*, 811
fresh air in, *Nov*, 817
isolation in, *Nov*, 812
oxygen therapy, *Nov*, 818
parenteral fluids in, *Nov*, 817
prophylaxis, *Nov*, 811
routine care, *Nov*, 823
serum treatment, *Nov*, 822
sleep and rest in, *Nov*, 814
transfusions in, *Nov*, 819
treatment, *Nov*, 814
lobar, oxygen therapy, *March* 1487
perforated gastric or duodenal ulcer and, differentiation, *July*, 199
pneumococcus, diagnosis, *Jan*, 1096
clinical considerations, *Jan*, 1096
types, and serum treatment, *Jan*, 1094
typing, *Jan*, 1097
Neufeld, *Jan*, 1097
respiratory rate, diagnostic value, *July*, 191
serum treatment, details of administration, *Jan*, 1100
effect on clinical course, *Jan*, 1104
indications and contraindications, *Jan*, 1105
precautions, *Jan*, 1101
reactions and their management *Jan*, 1102
relationship of pneumococcus types, *Jan*, 1093
Pneumoperitoneum due to other causes than perforated peptic ulcer, roentgen study, *March*, 1428
due to perforated peptic ulcer, roentgen demonstration of, *March*, 1423
valvular, roentgen diagnosis, *March*, 1429
Pneumothorax for diagnosis in bronchiectasis, *Jan*, 1044
in treatment of bronchiectasis, *Jan*, 1045

Poliomyelitis, anterior *July* 1
abortive cases *July* 6 18
active and passive motion beginning *July* 59
acute stage mechanical therapeusis *July* 45 54 56
adenopathy secondary to *Nov* 646
ascending type *July* 22
ataxic type *July* 22
autarcesis in *July* 8 35
blood in *July* 23
transfusions in *July* 44
Brudzinski's neck reflex, *July* 26
case investigation *July* 26
cerebral type *July* 22
cerebrospinal fluid in *July* 23
chronic stage mechanical therapeusis *July* 57 58
corrective treatment *July* 51
descending type *July* 22
diagnosis *July* 15
differential diagnosis *July* 23
dromedary cases *July* 19
epidemiology *July* 5
etiology *July* 3
fatigue in avoiding *July* 58
fever in *July* 16
first stage *July* 16
conditions simulating *July* 23
headache in, *July* 17 19
immobilization in *July* 45 55
immunity *July* 6 7
immunization *July* 35
incidence *July* 6–11
incubation period *July* 4 16
invasive stage *July* 16
conditions simulating *July* 23
massage in *July* 57
mechanical therapeusis *July* 51
meningeal irritation stage *July* 19
conditions simulating *July* 24
meningismus and differentiation *July* 24
mode of infection *July* 31
morning paralysis in *July* 15
mortality *July* 12 49
muscle equilibrium in earliest stage *July* 54
reeducation *July* 58
relaxation after beginning of paralysis *July* 56
paralysis in distribution *July* 13
results *July* 22
stage of *July* 19
conditions simulating *July* 5
Poliomyelitis anterior paralysis in treatment corrective *July* 51
early *July* 45 51
pathogenesis, *July* 5
physiologic rest in *July* 54
prognosis *July* 49
prophylaxis, *July* 31
consideration of community *July* 31
of individual *July* 33
quarantine in *July* 41
reflexes in *July* 21
respirator in use of *July* 46
saline bath in *July* 57
second stage, *July* 18
conditions simulating *July* 24
serum prophylaxis *July* 35
treatment *July* 41
spasticity and rigidity of back in *July* 18 27 28
special types *July* 22
spinal deformities of backache due to *March* 1349
surgery in *July* 61
susceptibility stigmata of *July* 11
symposium on *July* 1
symptomatology *July* 15
third stage *July* 19
conditions simulating *July* 25
tonsillectomy predisposing to *July* 34
transmission of *July* 32 33
treatment *July* 41
corrective, *July* 51
of bulbar involvement *July* 46
of pharyngeal paralysis *July* 4
of respiratory paralysis *July* 46
of skeletal paralysis *July* 45
miscellaneous *July* 45
orthopedic nonsurgical *July* 51
serum *July* 41
transfusions *July* 44
virus of *July* 3 4
weight bearing after *July* 61
Pollen asthma treatment *July* 137
Polyarthritis acute heart lesion in clinical significance *Nov* 63
Polyglandular hyperplasia *March* 1341
Polypi carcinomatous of stomach causing intussusception *Sept* 532
of cervix leukemia due to *May* 1170
Polyps multiple treatment *May* 1112

Polyps of uterus as cause of leukorrhea, *May*, 1699
Pooled adult serum in prophylaxis of anterior poliomyelitis, *July*, 35
in treatment of anterior poliomyelitis, *July*, 43
convalescent serum in treatment of anterior poliomyelitis, *July*, 43
Popliteal artery, spontaneous false aneurysm of, *Sept*, 613
Postmenopausal bleeding, *Nov*, 773
Postoperative pulmonary complications, oxygen therapy, *March*, 1488
Postural correction, study of relation of chronic duodenal stasis and visceroptosis by, *July*, 155
defects in production of backache, *Jan*, 980 *March*, 1345
of degenerative arthritis, *Jan*, 950, 975–980
of foot strain, *Jan*, 983
of knee strain, *Jan*, 983
hypotension with syncope, *Sept*, 585
treatment, *Sept*, 591
Posture, good and bad, *Jan*, 977, 978
in chronic arthritis, *July*, 127
poor, causes of, *Jan*, 977
Potencies and hereditary diabetes, *July*, 274
Preclimacteric bleeding *Nov*, 773
treatment, *Nov*, 783
Precocious puberty, *Nov*, 773
and virilism, *March*, 1462
treatment, *Nov*, 783
systoles, treatment, *May*, 1549
Preeclampsia, *July*, 298, 299
treatment, *July*, 301
Pregnancy, ectopic, rupture of, as surgical emergency, *July*, 69
edema of, treatment, *March*, 1501
hypoglycemia of, treatment, *March*, 1495
pyelitis of, treatment, *March*, 1503
systemic complications, treatment, *March*, 1495
Premature puberty, *Nov*, 773 *March*, 1462
treatment, *Nov*, 783
Premenstrual hypertrophy as cause of leukorrhea, *May*, 1698
tension, *Nov*, 773
treatment, *Nov*, 787
Progestin, *Jan*, 1146, 1147
dosage, *Jan*, 1156
Progynon, *Jan*, 1146
in adiposogenital dystrophy, *July*, 250
Prolan, *Jan*, 1144, 1146
Prolan, dosage, *Jan*, 1156
in treatment of adiposogenital dystrophy, *July*, 248
Proliferative arthritis, *July*, 112, 117
physiotherapy in, *Jan*, 1015
Proluton B, *Jan*, 1146, 1156
Proteinuria, Bence Jones, complicating hyperparathyroidism, *Jan*, 1109
Pseudoleukemia, *Nov*, 673
Psychiatric maladjustments causing difficulty in diagnosis, *July*, 329
Psychic manifestations in mucous colitis, *Nov*, 897
treatment, *Nov*, 907
Psychopath, sexual, with insane ancestry, *Sept*, 543
Pubertas praecox, *Nov*, 773
Puberty bleeding, *Nov*, 773
treatment, *Nov*, 783
with moccasin venom, *Nov*, 784
precocious, *Nov* 773, *March*, 1462
treatment, *Nov*, 783
Puerperal sepsis, treatment with immune serum, *March*, 1395
toxemia *July*, 298
Pulmonary complications, postoperative, oxygen therapy *March*, 1488
cyanosis, *Sept*, 601
peripheral cyanosis and, differentiation, *Sept*, 601
efficiency, vital capacity as test of, present status, *May*, 1685
tuberculosis, erythrocytic sedimentation test in, value *Nov*, 914
unusual types, *Sept*, 459
valvulitis with mitral involvement in rheumatic heart disease, *July*, 233
Pulsus alternans, digitalis therapy *May*, 1592
treatment, *May*, 1559
arrythmicus, *July*, 343
irregularis perpetuus, *July*, 343
Purpura, Henoch's, with erythema nodosum, hypersensitivity in, *March*, 1237
recurrent, of allergic origin, *March*, 1260
Pyelitis of pregnancy treatment, *March*, 1501
Pyramidon in rheumatic heart disease in children, *May*, 1563

Quelling-reaktion of Neufeld, *Jan*, 1097
Quinidine therapy in auricular fibrillation and flutter, *July*, 349 *Nov*, 751 *May*, 1554

RADICULAR syndrome simulating angina pectoris *March* 1266 1270
Radiotherapeutic sterilization in menorrhagia and metrorrhagia *Nov.*, 786
Radium treatment of hyperesthetic rhinitis, *March* 1250
Rectus muscles, increased tension causes of *July* 103
Reflexes in anterior poliomyelitis *July* 21
Regurgitation nervous, *Sept* 546
Renal. See *Kidney*
Respiration nerve mechanism of *July* 194
Respirator in anterior poliomyelitis *July* 46
Respiratory function vital capacity as test of present status *May* 1685
paralysis in anterior poliomyelitis *July* 20
treatment *July* 46
rate in pneumonia diagnostic value *July*, 191
Rest in chronic arthritis *July* 121
in chronic heart failure *Nov* 131
in pneumonia in children *Nov* 814
physiologic, in anterior poliomyelitis *July* 54
Retching attacks of in patient with melancholic heredity *Sept* 545
Reticulo-endothelium of lymph gland adenopathy originating primarily in *Nov* 669
function of *Nov* 639
Reticulosis aleukemic, *Nov* 673
Reticulum cell sarcoma of lymph nodes *Nov* 668
Retroversion of uterus dysmenorrhea due to, *March* 1281
Rheumatic arthritis in children *May* 1673
carditis treatment *Nov* 742
disease hypersensitivity in *March* 1231
endocarditis acute treatment *May* 1516
fever acute rheumatoid (infectious) arthritis and differentiation *Nov.*, 759
adenopathy secondary to *Nov* 645
complicating acute polyarthritis *Jan* 989
erythrocytic sedimentation test in value *Nov* 913
gout and differentiation *Jan* 1006
hypersensitivity in *March* 1240
heart disease See *Heart disease rheumatic*
Rheumatic pericarditis tuberculous pericarditis and differentiation *July* 215 216
Rheumatism *July* 107
Rheumatoid arthritis. See *Arthritis degenerative*
Rhinitis allergic, *March* 1234 1235 1245
hyperesthetic, *March* 1245
radium treatment *March* 1250
vasomotor *March* 1234 1245
Richter's hernia as surgical emergency *July* 16
Rickets spinal deformities of backache due to *March* 1380
Rigidity of back in anterior poliomyelitis *July* 21
Ringworm of allergic origin *March* 1254 1257 1258
Roentgen diagnosis of abdominal injuries *March* 1437
of acute abdominal affections *March* 1421
appendicitis, *March* 1436
of conditions causing pneumoperitoneum other than perforated peptic ulcer *March* 1428
of extra abdominal lesions simulating acute surgical affection *March* 1439
of intestinal obstruction *March* 1429
of perforated peptic ulcer *March* 1423
of valvular pneumoperitoneum *March* 1431
treatment of adiposogenital dystrophy *July* 240
of carcinomatous lymphadenopathy *Nov* 18
of chronic lymphatic leukemia *Nov* 98
of Hodgkin's disease *Nov* 15
of lymphadenopathies *Nov* 93
of lymphosarcoma *Nov* 12
of mycosis fungoides *Nov* 11
of myelogenous leukemia *Nov* 121
of persistent enlargement of thymus in infants *Nov.*, 697
of tuberculous laryngitis *March* 1380
lymphadenitis *Nov* 96
stimulating in amenorrhea *Nov* 57
Roll pelvic *Jan* 955
Rubella adenopathy secondary to *Nov* 645
Ruptured appendiceal abscess *Nov* 73

Rupture of bladder, *July*, 70
of ectopic pregnancy, *July*, 69
of gallbladder, *July*, 75
of kidney, *July*, 68
of liver, *July*, 66
of mesentery, *July*, 69
of peptic or typhoid ulcer, *July*, 73
of spleen, *July*, 67

SACRO-ILIAC joint, degenerative arthritis of, *Jan*, 961
lumbosacral arthritis and, differentiation, *Jan*, 962
strain, *Jan*, 961, 980
Salicylates in rheumatic heart disease in children, *May*, 1561
Saline bath in anterior poliomyelitis, *July*, 57
Salyrgan in myocardial failure in children, *May*, 1567
Sarcoma, Ewing's reticulum cell, of lymph nodes, *Nov*, 668
Sauerbruch and Hermannsdorfer diet in tuberculosis of skin, *July*, 325
Scarlet fever, adenopathy secondary to, *Nov*, 644
Schools for cardiac children, *March*, 1478
Sciatica, *Jan*, 980
Scratch tests in allergic diseases, *March*, 1230
Scrofuloderma, *July*, 319
treatment *July*, 324
Scrofulous gummata, *July*, 319
Sedatives in chorea, *Jan*, 1089
in rheumatic heart disease in children, *May*, 1561
Sedimentation test, erythrocytic, application in special problems, *Nov*, 912
practical value *Nov*, 911
technic, *Nov*, 912
Sensitization dermatitis, *March*, 1254
Sepsis puerperal, treatment with immune serum, *March*, 1395
Serous membranes, inflammatory changes in, with long continued fever and eventual glomerulonephritis, *Jan*, 1023
Serum, immune, in treatment of puerperal sepsis, *March*, 1395
prophylaxis of anterior poliomyelitis, *July*, 35
sickness, following administration of erysipelas antitoxin, *Nov*, 864
treatment of anterior poliomyelitis, *July*, 41
of pneumonia See under *Pneumonia*
Sex chromosomes in transmission of diabetes, *July*, 273
Sexual psychopath with insane ancestry, *Sept*, 543
Shaggy mucus in biliary drainage, *July*, 172
Shaw types of uterine bleeding, *Jan*, 1161
Shortness of breath in rheumatic heart disease in children, *May*, 1560
Shoulder joint, arthritis of, *Jan*, 953
physiotherapy in, *Jan*, 1021
Shoulders, deformities in, prevention in arthritis, *Sept*, 553
Sigmoid, intussusception of, due to malignant polyp, *Sept*, 539
Silicosis, *Nov*, 686
Simmonds' disease, *July*, 253
Sino auricular block and ventricular escapes in syphilitic heart disease with bundle branch block and vagus overactivity of sinus node, *March*, 1383
Sinus arrhythmia, treatment, *May*, 1547
Sinusitis, acute, treatment by antiseptics, *July*, 373
by atropine or belladonna, *July*, 372
by general practitioner, *July* 363
by nasal drops, *July*, 368, 370
by vaccines *July*, 372
Sistomensin, *Jan*, 1146
Skeletal paralysis in anterior poliomyelitis early treatment, *July*, 45
Skin, diseases of, allergy in, *March* 1253
reactions in allergic diseases, *March*, 1230
tests in bronchial asthma, *July*, 134
to determine presence of visceral infection, *July*, 145
tuberculosis of, *July*, 311
identification of tubercle bacillus, *July*, 311
methods of infection, *July*, 311
treatment, *July*, 323
types, *July*, 311
Smith sign in tuberculous thoracic glands, *Nov*, 650
Sodium perborate in Vincent's disease, *May*, 1718
Spasticity of back in anterior poliomyelitis, *July*, 18, 27, 28
Spina bifida in newborn, *March*, 1409
Spinal drainage in eclampsia, *July*, 303, 304
epidural area, abscess of, *July*, 287
Spine, arthritis of, *Jan*, 955
backache due to, *March*, 1347

Spine, arthritis of cervical portion *Jan* 959
differential diagnosis *Jan* 955
dorsal portion *Jan* 960
lumbar portion *Jan* 960
prevention of deformities *Sept* 559
physiotherapy in *Jan* 1021
symptoms and signs *Jan* 95
thoracic portion prevention of deformities *Sept* 558
deformities due to poliomyelitis backache due to *March* 1349
to posture backache due to *March* 1345
to rickets backache due to *March* 1350
to tuberculosis backache due to *March* 1351
nonsurgical treatment *March* 1352
Spleen enlargement of metabolic disturbances causing *Nov* 656
rupture of as surgical emergency *July* 67
Splenic disease pain in *July* 100
Splenomegaly of indeterminate type *Sept* 377
with intermittently painful joints and anemia three cases *Jan* 1053
Spondylitis *July* 115
Sprue chronic pancreatitis and differentiation *Sept* 526
tropical liver and stomach preparation (extralin) in *Sept* 388
Sputum blood in as symptom of acute heart failure with mitral stenosis *Nov* 917
Stasis duodenal and ureteroptosis study of relation by use of postural correction *July* 155
Static defects in production of degenerative arthritis *Jan* 950 955 959
Status anginosus *May* 1511
Stenosis cervical and leukorrhea *May* 1406
mitral acute heart failure in hemoptysis as symptom *Nov* 917
Sterilization radiotherapeutic in menorrhagia and metrorrhagia *Nov* 786
Stethoscope test for determining position of duodenal tube *July* 163
Still's disease *Jan* 1059
Stomach and liver preparation (extralin) in pernicious anemia *Sept* 385
carcinoma of a cause of indigestion *July* 89
found at operation after prolonged medical treatment of ulcer *Sept* 505
gastric pain in *July* 99
inoperable anemia in treatment *Jan* 1193
diseases of epigastric distress in *March* 1388
detention of pain in *July* 91
functional diseases of as cause of indigestion *July* 85
a cause of pain *July* 9
organic diseases of pain in *July* 95
pain in *July* 93
causes of *July* 91
digestive time table in diagnosis and *July* 101 103
in acute abdominal condition *July* 95
in carcinoma of stomach *July* 99
in functional diseases of stomach *July* 87
in gastric distention *July* 91
in organic diseases of stomach *July* 95 98
in peptic ulcer *July* 98
tenderness in localized causes of *July* 102
ulcer of a cause of indigestion

Stramonium datura in chorea, *Jan*, 1090
Strangulation, abdominal, as surgical emergency, *July*, 76
Stridor in newborn, *March*, 1413
Strongyloides hominis in biliary drainage specimens, *July*, 173
Strümpell Marie type of spondylitis, *July*, 115
Subarachnoid hemorrhage complicating rheumatic heart disease, *July*, 307
Subclavian artery, left, arteriosclerotic occlusion of, *Sept*, 629
Sulphur granules, *May*, 1738
  in treatment of acne vulgaris, *March*, 1466
Supplemental feeding of newborn, *March*, 1415
Suprarenal cortex, tumors of, in children, *March*, 1462
  gland, carcinoma of, pluriglandular syndrome associated with, *March*, 1367
  tumor with hirsutism and diabetes, *July*, 261
Suprarenocortical syndrome, *March*, 1374
  and pituitary basophilism, *Sept*, 411
Surgical abdomen, extra abdominal lesions simulating, x ray diagnosis in, *March*, 1439
  emergencies of abdomen, *July*, 63
Sydenham's chorea, *Jan*, 1081
Sympathectomy for early malignant hypertension, *Sept*, 577
Sympathicotonia, treatment, *May*, 1548
Syncope in orthostatic hypotension, *Sept*, 585
  treatment, *Sept*, 591
Syndrome, Felty's, *Jan*, 1062
  Fröhlich's, *July*, 243 *Jan*, 1194
  endocrine therapy, *March*, 1452
  peptic ulcer, atypical, *March*, 1287
  pluriglandular associated with carcinoma of right suprarenal gland, *March*, 1367
  suprarenocortical, *March*, 1374
  and pituitary basophilism, *Sept*, 411
Synovial membranes, inflammatory changes in, with long continued fever and eventual glomerulonephritis, *Jan*, 1023
Syphilis in newborn, *March*, 1411
  of heart, treatment, *May*, 1533
  of larynx, tuberculosis of larynx and, differentiation, *March*, 1378
Syphilitic arthritis *Jan*, 994
Syphilitic endocarditis, treatment, *May*, 1523
  heart disease with bundle branch block, sino-auricular block and ventricular escapes, vagus overactivity of sinus node demonstrated, *March*, 1383
  lymph glands, *Nov*, 654
Systoles, precocious, treatment, *May*, 1549

Tabes mesenraica, *Nov*, 652
Tachycardia, paroxysmal, digitalis therapy, *May*, 1552, 1592
  treatment, *Nov*, 752, *May*, 1549, 1551
Tamponade, cardiac, *May*, 1524
Temperament of children, *May*, 1668
Temple treatment of eclampsia, *July*, 297
Temporomandibular joints, osteo-arthritis of, *Jan*, 952
Tenderness and rigidity in acute appendicitis, *March*, 1490
  epigastric, localized, causes of, *July*, 102
Tension, premenstrual, *Nov*, 773
  treatment, *Nov*, 787
Theelin, *Jan*, 1146
  dosage, *Jan*, 1156
  in adiposogenital dystrophy, *July*, 250
Theelol, *Jan*, 1146
Theocin in diabetes insipidus, *May*, 1608
Therapeutic paradox in arsphenamine therapy of syphilis of heart, *May*, 1533
Thirst fever in newborn, *March*, 1413
Thoracic glands, tuberculous, *Nov*, 649
  spine, deformities in, prevention in arthritis, *Sept*, 558
Thorax, deformities in, prevention in arthritis, *Sept*, 558
  referred pain from, to epigastric region, *March*, 1288
Thrombo angiitis obliterans with common types of pain, *Sept*, 623
Thrombocytopenia, subleukemic lymphatic leukemia and, differentiation, *Nov*, 659
Thrombophlebitis, idiopathic, recurrent, of legs, *Sept*, 597
Thrombosis, coronary See *Coronary thrombosis*
  mesenteric, as surgical emergency, *July*, 77
Thrush in newborn, *March*, 1419
Thymus, delayed involution or hyperplasia of, *Nov*, 693

Thymus enlarged as cause of death in newborn *March* 1410
persistent enlargement in infants *Nov* 124
treatment *Nov* 725
Thyroid extracts in obesity *Jan* 1199
gland disease of with cardiac complications two cases *Jan* 1027
relation to Graves disease *Nov* 791
tumor of Hodgkin's disease and differentiation *Nov* 618
therapy in adiposogenital dystrophy *July* 248
in juvenile hypothyroidism *March* 1443
Thyrotoxicosis in relation to status lymphaticus *Nov* 698
Tissue extracts effect on intermittent claudication *Sept* 609
Tonsillectomy, recent predisposing to anterior poliomyelitis *July* 34
Tophi *Jan* 1010
Toxemia hepato-intestinal duodenal drainage in *July* 174
intestinal in mucous colitis *Nov* 826
with constipation colonic irrigations in *May* 1615 1619
puerperal *July* 208
Traction in chronic infectious arthritis *Sept* 569
Tractus supraopticohypophyseus *May* 1598 1600
Transduodenal lavage for intestinal worms *July* 115
Transfusions in anterior poliomyelitis *July* 44
in chronic arthritis *July* 128
in pneumonia in children *Nov* 819
Trauma mechanical acute effect on joints *Jan* 913
chronic effect on joints *Jan* 914
importance in joint pain *Jan* 971
Traumatism abdominal as surgical
Tuberculosis cutis orificialis *July* 320
vera *July* 320
in newborn *March* 1412
luposa *July* 312
miliary *July* 322
pericardial See *Pericarditis tuberculous*
pulmonary erythrocytic sedimentation test in value *Nov* 914
unusual types *Sept* 459
spinal deformities of backache due to *March* 1351
ulcerosa *July* 320
vegetans et framboesiformis *July* 322
verrucosa *July* 321
treatment *July* 324
Tuberculous abscess of lung *Sept* 448
chancre *July* 321
intra-abdominal glands *Nov* 651
laryngitis progressive diagnosis and treatment *March* 1377
lymphadenitis treatment *Nov* 705
lymphoma diffuse *Nov* 652
pericarditis *July* 201 See also *Pericarditis tuberculous*
pleurisy with probable chronic glomerulonephritis *Sept* 395
superficial glands *Nov* 648
thoracic glands *Nov* 649
Tularemia adenopathy secondary to *Nov* 645
Tumors of ovary in children *March* 1462
of suprarenal cortex in children *March* 1467
of thyroid gland Hodgkin's disease and differentiation *Nov* 618
suprarenal with hirsutism and diabetes *July* 261
Typhoid fever a leukopathy secondary to *Nov* 616
ulcer perforation of as surgical emergency *July* 53
Typhoid paratyphoid vaccine in chorea *Jan* 1090

Ulcerative conditions of colon, treatment, *March*, 1319
pharyngitis, *May*, 1711
Umbilical hernia in newborn, *March*, 1409
Uremia, *Nov*, 878
diet in, *Nov*, 878
medicinal treatment *Nov*, 881
Urticaria of allergic origin, *March*, 1260
Uterine bleeding, hormone therapy *Jan*, 1161
Uterus lesions of, as cause of leukorrhea *May*, 1698
retroversion of, dysmenorrhea due to, *March*, 1281

Vaccines in acute sinusitis, *July*, 372
in bronchial asthma, *July*, 139
in chronic arthritis *July* 129
in nonspecific ulcerative colitis, *March* 1325
typhoid paratyphoid, in chorea, *Jan*, 1090
Vagina, lesions of leukorrhea due to, *May*, 1707
Vaginal lymphosarcoma, *Nov*, 667
Vaginitis, Monilia, *May*, 1710
senile, leukorrhea due to *May* 1707
Trichomonas vaginalis, leukorrhea due to, *May*, 1707
Vagotonia, treatment, *May*, 1548
Vagus nucleus in medulla oblongata, hyperplasia of in status lymphaticus, *Nov*, 698
paralysis in anterior poliomyelitis *July*, 21
Valvular heart disease chronic rheumatic *Nov*, 744
pneumoperitoneum roentgen diagnosis, *March*, 1429
Valvulitis, mitral and pulmonary, in rheumatic heart disease *July*, 233
Van Slyke Binger vital capacity test of respiratory function, *May* 1688
Vascular disease complicating gout, *Jan* 1010
Vasomotor collapse in pneumonia in children treatment, *Nov* 825
rhinitis *March*, 1234, 1245
Vasopressin, *July* 240
Venesection in cardiac edema in children, *May*, 1568
in eclampsia *July*, 304
Venom, moccasin, in puberty bleeding, *Nov*, 784
Ventricular escapes and sino-auricular block in syphilitic heart disease with bundle branch block and vagus overactivity of sinus node *March*, 1383
Ventricular precocious systoles, treatment, *May*, 1550
Vincent's angina, *May*, 1711, 1712
disease, *May*, 1711
diagnosis, *May*, 1716
treatment, *May*, 1717
stomatitis, *May*, 1712
Vioform in intestinal amebiasis, *Nov*, 857
Virilism, precocious, *March*, 1462
Virus of infantile paralysis, *July*, 3, 4
Visceral infection, evidences of, *July*, 143
injury from abdominal contusions, *July* 64
Visceroptosis and duodenal stasis study of relationship by use of postural correction, *July*, 155
Vital capacity as test of pulmonary efficiency, present status, *May*, 1685
Volvulus roentgen diagnosis *March*, 1436
Vomiting, gastric with alkalosis and dehydration in childhood *Jan*, 1218
in acute appendicitis, *March*, 1490

Water supply and anterior poliomyelitis, *July*, 32
test for determining position of duodenal tube, *July*, 169
Weight bearing after anterior poliomyelitis, *July* 60
incorrect, as cause of joint pain and arthritis *Jan* 975–980
loss, physiologic, in newborn, *March*, 1415
Whole blood, adult, in prophylaxis of anterior poliomyelitis, *July*, 35 36
reactions, *July*, 37
Whooping cough pneumonia following *Sept*, 455
Worms, intestinal transduodenal lavage for *July*, 175
Wounds of abdominal walls as surgical emergencies, *July*, 71
Wrist joint, arthritis of *Jan* 954
physiotherapy in, *Jan*, *1020*
Wrists deformities in prevention in arthritis *Sept*, 555

Xanthoma diabeticorum *Nov*, 690
x Ray See *Roentgen*

Yeast infections of vagina, *May* 1710